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DEX0285_163   Antigenicity Index(Jameson-Wolf)
    positions   AI avg length
    10-24   1.21   15
DEX0285_167   Antigenicity Index(Jameson-Wolf)
5   positions   AI avg length
    35-54   1.30   20
DEX0285_169   Antigenicity Index(Jameson-Wolf)
    positions   AI avg length
    92-104   1.03   13
10 DEX0285_183   Antigenicity Index(Jameson-Wolf)
    positions   AI avg length
    14-56   1.12   43
DEX0285_184   Antigenicity Index(Jameson-Wolf)
    positions   AI avg length
15 76-85   1.08   10
DEX0285_196   Antigenicity Index(Jameson-Wolf)
    positions   AI avg length
    14-28   1.10   15
DEX0285_197   Antigenicity Index(Jameson-Wolf)
20 positions   AI avg length
    82-104   1.27   23
    57-69   1.27   13
    138-151   1.21   14
    111-131   1.06   21
25 DEX0285_199   Antigenicity Index(Jameson-Wolf)
    positions   AI avg length
    5-19   1.01   15
DEX0285_203   Antigenicity Index(Jameson-Wolf)
    positions   AI avg length
30 36-46   1.00   11

In addition, the following helical regions were also assigned:

DEX0275_33 PredHel=1   Topology=i69-91o

DEX0275_42 PredHel=1   Topology=i7-29o

DEX0275_44 PredHel=1   Topology=i7-26o

DEX0275_47 PredHel=1   Topology=i44-66o

DEX0275_48 PredHel=1   Topology=o20-42i

5

Example 6:   Method of Determining Alterations in a Gene Corresponding to a Polynucleotide

RNA is isolated from individual patients or from a family of individuals that have a phenotype of interest. cDNA is then generated from these RNA samples using

10   protocols known in the art. *See,* Sambrook (2001), *supra.* The cDNA is then used as a template for PCR, employing primers surrounding regions of interest in SEQ ID NO: 1 through 29. Suggested PCR conditions consist of 35 cycles at 95°C for 30 seconds; 60-120 seconds at 52-58°C; and 60-120 seconds at 70°C, using buffer solutions described in Sidransky *et al., Science* 252(5006): 706-9 (1991). *See also* Sidransky *et al.,*

15   *Science* 278(5340): 1054-9 (1997).

PCR products are then sequenced using primers labeled at their 5' end with T4 polynucleotide kinase, employing SequiTherm Polymerase. (Epicentre Technologies). The intron-exon borders of selected exons is also determined and genomic PCR products analyzed to confirm the results. PCR products harboring suspected mutations are then

20   cloned and sequenced to validate the results of the direct sequencing. PCR products is cloned into T-tailed vectors as described in Holton *et al., Nucleic Acids Res.,* 19: 1156 (1991) and sequenced with T7 polymerase (United States Biochemical). Affected individuals are identified by mutations not present in unaffected individuals.

Genomic rearrangements may also be determined. Genomic clones are

25   nick-translated with digoxigenin deoxyuridine 5' triphosphate (Boehringer Manheim), and FISH is performed as described in Johnson *et al., Methods Cell Biol.* 35: 73-99 (1991). Hybridization with the labeled probe is carried out using a vast excess of human cot-1 DNA for specific hybridization to the corresponding genomic locus.

Chromosomes are counterstained with 4,6-diamino-2-phenylidole and propidium

30   iodide, producing a combination of C-and R-bands. Aligned images for precise mapping are obtained using a triple-band filter set (Chroma Technology, Brattleboro, VT) in combination with a cooled charge-coupled device camera (Photometrics, Tucson, AZ)

and variable excitation wavelength filters. *Id.* Image collection, analysis and chromosomal fractional length measurements are performed using the ISee Graphical Program System. (Inovision Corporation, Durham, NC.) Chromosome alterations of the genomic region hybridized by the probe are identified as insertions, deletions, and
5   translocations. These alterations are used as a diagnostic marker for an associated disease.

Example 7:   Method of Detecting Abnormal Levels of a Polypeptide in a Biological Sample

Antibody-sandwich ELISAs are used to detect polypeptides in a sample,
10   preferably a biological sample. Wells of a microtiter plate are coated with specific antibodies, at a final concentration of 0.2 to 10 μg/ml. The antibodies are either monoclonal or polyclonal and are produced by the method described above. The wells are blocked so that non-specific binding of the polypeptide to the well is reduced. The coated wells are then incubated for > 2 hours at RT with a sample containing the
15   polypeptide. Preferably, serial dilutions of the sample should be used to validate results. The plates are then washed three times with deionized or distilled water to remove unbound polypeptide. Next, 50 μl of specific antibody-alkaline phosphatase conjugate, at a concentration of 25-400 ng, is added and incubated for 2 hours at room temperature. The plates are again washed three times with deionized or distilled water to remove
20   unbound conjugate. 75 μl of 4-methylumbelliferyl phosphate (MUP) or p-nitrophenyl phosphate (NPP) substrate solution are added to each well and incubated 1 hour at room temperature.

The reaction is measured by a microtiter plate reader. A standard curve is prepared, using serial dilutions of a control sample, and polypeptide concentrations are
25   plotted on the X-axis (log scale) and fluorescence or absorbance on the Y-axis (linear scale). The concentration of the polypeptide in the sample is calculated using the standard curve.

Example 8: Formulating a Polypeptide

The secreted polypeptide composition will be formulated and dosed in a fashion
30   consistent with good medical practice, taking into account the clinical condition of the individual patient (especially the side effects of treatment with the secreted polypeptide

alone), the site of delivery, the method of administration, the scheduling of administration, and other factors known to practitioners. The "effective amount" for purposes herein is thus determined by such considerations.

As a general proposition, the total pharmaceutically effective amount of secreted
5   polypeptide administered parenterally per dose will be in the range of about 1 , μg/kg/day to 10 mg/kg/day of patient body weight, although, as noted above, this will be subject to therapeutic discretion. More preferably, this dose is at least 0.01 mg/kg/day, and most preferably for humans between about 0.01 and 1 mg/kg/day for the hormone. If given continuously, the secreted polypeptide is typically administered at a dose rate of about 1
10 μg/kg/hour to about 50 mg/kg/hour, either by 1-4 injections per day or by continuous subcutaneous infusions, for example, using a mini-pump. An intravenous bag solution may also be employed. The length of treatment needed to observe changes and the interval following treatment for responses to occur appears to vary depending on the desired effect.

15   Pharmaceutical compositions containing the secreted protein of the invention are administered orally, rectally, parenterally, intracistemally, intravaginally, intraperitoneally, topically (as by powders, ointments, gels, drops or transdermal patch), bucally, or as an oral or nasal spray. "Pharmaceutically acceptable carrier" refers to a non-toxic solid, semisolid or liquid filler, diluent, encapsulating material or formulation
20 auxiliary of any type. The term "parenteral" as used herein refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The secreted polypeptide is also suitably administered by sustained-release systems. Suitable examples of sustained-release compositions include semipermeable
25 polymer matrices in the form of shaped articles, e. g., films, or microcapsules. Sustained-release matrices include polylactides (U. S. Pat. No.3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma-ethyl-L-glutamate (Sidman, U. et al., Biopolymers 22: 547-556 (1983)), poly (2-hydroxyethyl methacrylate) (R. Langer et al., J. Biomed. Mater. Res. 15: 167-277 (1981), and R. Langer, Chem. Tech. 12: 98-105 (1982)), ethylene vinyl
30 acetate (R. Langer et al.) or poly-D- (-)-3-hydroxybutyric acid (EP 133,988). Sustained-release compositions also include liposomally entrapped polypeptides. Liposomes containing the secreted polypeptide are prepared by methods known per se: DE Epstein

et al., Proc. Natl. Acad. Sci. USA 82: 3688-3692 (1985); Hwang et al., Proc. Natl. Acad.
Sci. USA 77: 4030-4034 (1980); EP 52,322; EP 36,676; EP 88,046; EP 143,949; EP
142,641; Japanese Pat. Appl. 83-118008; U. S. Pat. Nos. 4,485,045 and 4,544,545; and
EP 102,324. Ordinarily, the liposomes are of the small (about 200-800 Angstroms)

5   unilamellar type in which the lipid content is greater than about 30 mol. percent
cholesterol, the selected proportion being adjusted for the optimal secreted polypeptide
therapy.

For parenteral administration, in one embodiment, the secreted polypeptide is
formulated generally by mixing it at the desired degree of purity, in a unit dosage

10   injectable form (solution, suspension, or emulsion), with a pharmaceutically acceptable
carrier, I. e., one that is non-toxic to recipients at the dosages and concentrations
employed and is compatible with other ingredients of the formulation.

For example, the formulation preferably does not include oxidizing agents and
other compounds that are known to be deleterious to polypeptides. Generally, the

15   formulations are prepared by contacting the polypeptide uniformly and intimately with
liquid carriers or finely divided solid carriers or both. Then, if necessary, the product is
shaped into the desired formulation. Preferably the carrier is a parenteral carrier, more
preferably a solution that is isotonic with the blood of the recipient. Examples of such
carrier vehicles include water, saline, Ringer's solution, and dextrose solution. Non-

20   aqueous vehicles such as fixed oils and ethyl oleate are also useful herein, as well as
liposomes.

The carrier suitably contains minor amounts of additives such as substances that
enhance isotonicity and chemical stability. Such materials are non-toxic to recipients at
the dosages and concentrations employed, and include buffers such as phosphate, citrate,

25   succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic
acid; low molecular weight (less than about ten residues) polypeptides, e. g., polyarginine
or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic
polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid,
aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates

30   including cellulose or its derivatives, glucose, manose, or dextrins; chelating agents such
as EDTA; sugar alcohols such as mannitol or sorbitol; counterions such as sodium;
and/or nonionic surfactants such as polysorbates, poloxamers, or PEG.

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The secreted polypeptide is typically formulated in such vehicles at a concentration of about 0.1 mg/ml to 100 mg/ml, preferably 1-10 mg/ml, at a pH of about 3 to 8. It will be understood that the use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of polypeptide salts.

5   Any polypeptide to be used for therapeutic administration can be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e. g., 0.2 micron membranes). Therapeutic polypeptide compositions generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

10   Polypeptides ordinarily will be stored in unit or multi-dose containers, for example, sealed ampules or vials, as an aqueous solution or as a lyophilized formulation for reconstitution. As an example of a lyophilized formulation, 10-ml vials are filled with 5 ml of sterile-filtered 1 % (w/v) aqueous polypeptide solution, and the resulting mixture is lyophilized. The infusion solution is prepared by reconstituting the lyophilized

15   polypeptide using bacteriostatic Water-for-Injection.

The invention also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions of the invention. Associated with such container (s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of

20   pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. In addition, the polypeptides of the present invention may be employed in conjunction with other therapeutic compounds.

Example 9:   Method of Treating Decreased Levels of the Polypeptide

It will be appreciated that conditions caused by a decrease in the standard or

25   normal expression level of a secreted protein in an individual can be treated by administering the polypeptide of the present invention, preferably in the secreted form. Thus, the invention also provides.a method of treatment of an individual in need of an increased level of the polypeptide comprising administering to such an individual a pharmaceutical composition comprising an amount of the polypeptide to increase the

30   activity level of the polypeptide in such an individual.

For example, a patient with decreased levels of a polypeptide receives a daily dose 0.1-100 µg/kg of the polypeptide for six consecutive days. Preferably, the

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polypeptide is in the secreted form. The exact details of the dosing scheme, based on administration and formulation, are provided above.

Example 10: Method of Treating Increased Levels of the Polypeptide

Antisense technology is used to inhibit production of a polypeptide of the present

5 invention. This technology is one example of a method of decreasing levels of a polypeptide, preferably a secreted form, due to a variety of etiologies, such as cancer.

For example, a patient diagnosed with abnormally increased levels of a polypeptide is administered intravenously antisense polynucleotides at 0.5, 1.0, 1.5, 2.0 and 3.0 mg/kg day for 21 days. This treatment is repeated after a 7-day rest period if the

10 treatment was well tolerated. The formulation of the antisense polynucleotide is provided above.

Example 11: Method of Treatment Using Gene Therapy

One method of gene therapy transplants fibroblasts, which are capable of expressing a polypeptide, onto a patient. Generally, fibroblasts are obtained from a

15 subject by skin biopsy. The resulting tissue is placed in tissue-culture medium and separated into small pieces. Small chunks of the tissue are placed on a wet surface of a tissue culture flask, approximately ten pieces are placed in each flask. The flask is turned upside down, closed tight and left at room temperature over night. After 24 hours at room temperature, the flask is inverted and the chunks of tissue remain fixed to the bottom of

20 the flask and fresh media (e. g., Ham's F12 media, with 10% FBS, penicillin and streptomycin) is added. The flasks are then incubated at 37°C for approximately one week.

At this time, fresh media is added and subsequently changed every several days. After an additional two weeks in culture, a monolayer of fibroblasts emerge. The

25 monolayer is trypsinized and scaled into larger flasks. pMV-7 (Kirschmeier, P. T. et al., DNA, 7: 219-25 (1988)), flanked by the long terminal repeats of the Moloney murine sarcoma virus, is digested with EcoRI and HindIII and subsequently treated with calf intestinal phosphatase. The linear vector is fractionated on agarose gel and purified, using glass beads.

30 The cDNA encoding a polypeptide of the present invention can be amplified using PCR primers which correspond to the 5'and 3'end sequences respectively as set forth in Example 1. Preferably, the 5'primer contains an EcoRI site and the 3'primer

includes a HindIII site. Equal quantities of the Moloney murine sarcoma virus linear
backbone and the amplified EcoRI and HindIII fragment are added together, in the
presence of T4 DNA ligase. The resulting mixture is maintained under conditions
appropriate for ligation of the two fragments. The ligation mixture is then used to

5   transform bacteria HB 101, which are then plated onto agar containing kanamycin for the
purpose of confirming that the vector has the gene of interest properly inserted.

The amphotropic pA317 or GP+am12 packaging cells are grown in tissue culture
to confluent density in Dulbecco's Modified Eagles Medium (DMEM) with 10% calf
serum (CS), penicillin and streptomycin. The MSV vector containing the gene is then

10   added to the media and the packaging cells transduced with the vector. The packaging
cells now produce infectious viral particles containing the gene (the packaging cells are
now referred to as producer cells).

Fresh media is added to the transduced producer cells, and subsequently, the
media is harvested from a 10 cm plate of confluent producer cells. The spent media,

15   containing the infectious viral particles, is filtered through a millipore filter to remove
detached producer cells and this media is then used to infect fibroblast cells. Media is
removed from a sub-confluent plate of fibroblasts and quickly replaced with the media
from the producer cells. This media is removed and replaced with fresh media.

If the titer of virus is high, then virtually all fibroblasts will be infected and no

20   selection is required. If the titer is very low, then it is necessary to use a retroviral vector
that has a selectable marker, such as neo or his. Once the fibroblasts have been efficiently
infected, the fibroblasts are analyzed to determine whether protein is produced.

The engineered fibroblasts are then transplanted onto the host, either alone or
after having been grown to confluence on cytodex 3 microcarrier beads.

25   **Example 12: Method of Treatment Using Gene Therapy-*In Vivo***

Another aspect of the present invention is using *in vivo* gene therapy methods to
treat disorders, diseases and conditions. The gene therapy method relates to the
introduction of naked nucleic acid (DNA, RNA, and antisense DNA or RNA) sequences
into an animal to increase or decrease the expression of the polypeptide.

30   The polynucleotide of the present invention may be operatively linked to a
promoter or any other genetic elements necessary for the expression of the polypeptide
by the target tissue. Such gene therapy and delivery techniques and methods are known

in the art, see, for example, WO 90/11092, WO 98/11779; U. S. Patent 5,693,622; 5,705,151; 5,580,859; Tabata H. et al. (1997) Cardiovasc. Res. 35 (3): 470-479, Chao J et al. (1997) Pharmacol. Res. 35 (6): 517-522, Wolff J. A. (1997) Neuromuscul. Disord. 7 (5): 314-318, Schwartz B. et al. (1996) Gene Ther. 3 (5): 405-411, Tsurumi Y. et al.

5   (1996) Circulation 94 (12): 3281-3290 (incorporated herein by reference).

The polynucleotide constructs may be delivered by any method that delivers injectable materials to the cells of an animal, such as, injection into the interstitial space of tissues (heart, muscle, skin, lung, liver, intestine and the like). The polynucleotide constructs can be delivered in a pharmaceutically acceptable liquid or aqueous carrier.

10   The term "naked" polynucleotide, DNA or RNA, refers to sequences that are free from any delivery vehicle that acts to assist, promote, or facilitate entry into the cell, including viral sequences, viral particles, liposome formulations, lipofectin or precipitating agents and the like. However, the polynucleotides of the present invention may also be delivered in liposome formulations (such as those taught in Felgner P. L. et

15   al. (1995) Ann. NY Acad. Sci. 772: 126-139 and Abdallah B. et al. (1995) Biol. Cell 85 (1): 1-7) which can be prepared by methods well known to those skilled in the art.

The polynucleotide vector constructs used in the gene therapy method are preferably constructs that will not integrate into the host genome nor will they contain sequences that allow for replication. Any strong promoter known to those skilled in the

20   art can be used for driving the expression of DNA. Unlike other gene therapies techniques, one major advantage of introducing naked nucleic acid sequences into target cells is the transitory nature of the polynucleotide synthesis in the cells. Studies have shown that non-replicating DNA sequences can be introduced into cells to provide production of the desired polypeptide for periods of up to six months.

25   The polynucleotide construct can be delivered to the interstitial space of tissues within the an animal, including of muscle, skin, brain, lung, liver, spleen, bone marrow, thymus, heart, lymph, blood, bone, cartilage, pancreas, kidney, gall bladder, stomach, intestine, testis, ovary, uterus, rectum, nervous system, eye, gland, and connective tissue. Interstitial space of the tissues comprises the intercellular fluid, mucopolysaccharide

30   matrix among the reticular fibers of organ tissues, elastic fibers in the walls of vessels or chambers, collagen fibers of fibrous tissues, or that same matrix within connective tissue ensheathing muscle cells or in the lacunae of bone. It is similarly the space occupied by

the plasma of the circulation and the lymph fluid of the lymphatic channels. Delivery to the interstitial space of muscle tissue is preferred for the reasons discussed below. They may be conveniently delivered by injection into the tissues comprising these cells. They are preferably delivered to and expressed in persistent, non-dividing cells which are

5   differentiated, although delivery and expression may be achieved in non-differentiated or less completely differentiated cells, such as, for example, stem cells of blood or skin fibroblasts. *In vivo* muscle cells are particularly competent in their ability to take up and express polynucleotides.

For the naked polynucleotide injection, an effective dosage amount of DNA or

10   RNA will be in the range of from about 0.05 μg/kg body weight to about 50 mg/kg body weight. Preferably the dosage will be from about 0.005 mg/kg to about 20 mg/kg and more preferably from about 0.05 mg/kg to about 5 mg/kg. Of course, as the artisan of ordinary skill will appreciate, this dosage will vary according to the tissue site of injection. The appropriate and effective dosage of nucleic acid sequence can readily be

15   determined by those of ordinary skill in the art and may depend on the condition being treated and the route of administration. The preferred route of administration is by the parenteral route of injection into the interstitial space of tissues. However, other parenteral routes may also be used, such as, inhalation of an aerosol formulation particularly for delivery to lungs or bronchial tissues, throat or mucous membranes of the

20   nose. In addition, naked polynucleotide constructs can be delivered to arteries during angioplasty by the catheter used in the procedure.

The dose response effects of injected polynucleotide in muscle *in vivo* is determined as follows. Suitable template DNA for production of mRNA coding for polypeptide of the present invention is prepared in accordance with a standard

25   recombinant DNA methodology. The template DNA, which may be either circular or linear, is either used as naked DNA or complexed with liposomes. The quadriceps muscles of mice are then injected with various amounts of the template DNA.

Five to six week old female and male Balb/C mice are anesthetized by intraperitoneal injection with 0.3 ml of 2.5% Avertin. A 1.5 cm incision is made on the

30   anterior thigh, and the quadriceps muscle is directly visualized. The template DNA is injected in 0.1 ml of carrier in a 1 cc syringe through a 27 gauge needle over one minute, approximately 0.5 cm from the distal insertion site of the muscle into the knee and about

0.2 cm deep. A suture is placed over the injection site for future localization, and the skin is closed with stainless steel clips.

After an appropriate incubation time (e. g., 7 days) muscle extracts are prepared by excising the entire quadriceps. Every fifth 15 um cross-section of the individual quadriceps muscles is histochemically stained for protein expression. A time course for protein expression may be done in a similar fashion except that quadriceps from different mice are harvested at different times. Persistence of DNA in muscle following injection may be determined by Southern blot analysis after preparing total cellular DNA and HIRT supernatants from injected and control mice.

The results of the above experimentation in mice can be use to extrapolate proper dosages and other treatment parameters in humans and other animals using naked DNA.

Example 13: Transgenic Animals

The polypeptides of the invention can also be expressed in transgenic animals. Animals of any species, including, but not limited to, mice, rats, rabbits, hamsters, guinea pigs, pigs, micro-pigs, goats, sheep, cows and non-human primates, e. g., baboons, monkeys, and chimpanzees may be used to generate transgenic animals. In a specific embodiment, techniques described herein or otherwise known in the art, are used to express polypeptides of the invention in humans, as part of a gene therapy protocol.

Any technique known in the art may be used to introduce the transgene (i. e., polynucleotides of the invention) into animals to produce the founder lines of transgenic animals. Such techniques include, but are not limited to, pronuclear microinjection (Paterson et al., Appl. Microbiol. Biotechnol. 40: 691-698 (1994); Carver et al., Biotechnology (NY) 11: 1263-1270 (1993); Wright et al., Biotechnology (NY) 9: 830-834 (1991); and Hoppe et al., U. S. Patent 4,873,191 (1989)); retrovirus mediated gene transfer into germ lines (Van der Putten et al., Proc. Natl. Acad. Sci., USA 82: 6148-6152 (1985)), blastocysts or embryos; gene targeting in embryonic stem cells (Thompson et al., Cell 56: 313-321 (1989)); electroporation of cells or embryos (Lo, 1983, Mol Cell. Biol. 3: 1803-1814 (1983)); introduction of the polynucleotides of the invention using a gene gun (see, e. g., Ulmer et al., Science 259: 1745 (1993); introducing nucleic acid constructs into embryonic pleuripotent stem cells and transferring the stem cells back into the blastocyst; and sperm mediated gene transfer (Lavitrano et al., Cell 57: 717-723 (1989); etc. For a review of such techniques, see Gordon,"Transgenic Animals," Intl.

Rev. Cytol. 115: 171-229 (1989), which is incorporated by reference herein in its entirety.

Any technique known in the art may be used to produce transgenic clones containing polynucleotides of the invention, for example, nuclear transfer into enucleated

5   oocytes of nuclei from cultured embryonic, fetal, or adult cells induced to quiescence (Campell et al., Nature 380: 64-66 (1996); Wilmut et al., Nature 385: 810813 (1997)).

The present invention provides for transgenic animals that carry the transgene in all their cells, as well as animals which carry the transgene in some, but not all their cells, I. e., mosaic animals or chimeric. The transgene may be integrated as a single transgene

10   or as multiple copies such as in concatamers, e. g., head-to-head tandems or head-to-tail tandems. The transgene may also be selectively introduced into and activated in a particular cell type by following, for example, the teaching of Lasko et al. (Lasko et al., Proc. Natl. Acad. Sci. USA 89: 6232-6236 (1992)). The regulatory sequences required for such a cell-type specific activation will depend upon the particular cell type of

15   interest, and will be apparent to those of skill in the art. When it is desired that the polynucleotide transgene be integrated into the chromosomal site of the endogenous gene, gene targeting is preferred. Briefly, when such a technique is to be utilized, vectors containing some nucleotide sequences homologous to the endogenous gene are designed for the purpose of integrating, via homologous recombination with chromosomal

20   sequences, into and disrupting the function of the nucleotide sequence of the endogenous gene. The transgene may also be selectively introduced into a particular cell type, thus inactivating the endogenous gene in only that cell type, by following, for example, the teaching of Gu et al. (Gu et al., Science 265: 103-106 (1994)). The regulatory sequences required for such a cell-type specific inactivation will depend upon the particular cell

25   type of interest, and will be apparent to those of skill in the art.

Once transgenic animals have been generated, the expression of the recombinant gene may be assayed utilizing standard techniques. Initial screening may be accomplished by Southern blot analysis or PCR techniques to analyze animal tissues to verify that integration of the transgene has taken place. The level of mRNA expression

30   of the transgene in the tissues of the transgenic animals may also be assessed using techniques which include, but are not limited to, Northern blot analysis of tissue samples obtained from the animal, in situ hybridization analysis, and reverse transcriptase-PCR

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(rt-PCR). Samples of transgenic gene-expressing tissue may also be evaluated immunocytochemically or immunohistochemically using antibodies specific for the transgene product.

Once the founder animals are produced, they may be bred, inbred, outbred, or
5   crossbred to produce colonies of the particular animal. Examples of such breeding strategies include, but are not limited to: outbreeding of founder animals with more than one integration site in order to establish separate lines; inbreeding of separate lines in order to produce compound transgenics that express the transgene at higher levels because of the effects of additive expression of each transgene; crossing of heterozygous
10 transgenic animals to produce animals homozygous for a given integration site in order to both augment expression and eliminate the need for screening of animals by DNA analysis; crossing of separate homozygous lines to produce compound heterozygous or homozygous lines; and breeding to place the transgene on a distinct background that is appropriate for an experimental model of interest.

15   Transgenic animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

20 **Example 14: Knock-Out Animals**

            Endogenous gene expression can also be reduced by inactivating or "knocking out" the gene and/or its promoter using targeted homologous recombination. (E. g., see Smithies et al., Nature 317: 230-234 (1985); Thomas & Capecchi, Cell 51: 503512 (1987); Thompson et al., Cell 5: 313-321 (1989); each of which is incorporated by
25 reference herein in its entirety). For example, a mutant, non-functional polynucleotide of the invention (or a completely unrelated DNA sequence) flanked by DNA homologous to the endogenous polynucleotide sequence (either the coding regions or regulatory regions of the gene) can be used, with or without a selectable marker and/or a negative selectable marker, to transfect cells that express polypeptides of the invention *in vivo*. In another
30 embodiment, techniques known in the art are used to generate knockouts in cells that contain, but do not express the gene of interest. Insertion of the DNA construct, via targeted homologous recombination, results in inactivation of the targeted gene. Such

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approaches are particularly suited in research and agricultural fields where modifications
to embryonic stem cells can be used to generate animal offspring with an inactive
targeted gene (e. g., see Thomas & Capecchi 1987 and Thompson 1989, supra).
However this approach can be routinely adapted for use in humans provided the

5   recombinant DNA constructs are directly administered or targeted to the required site *in
vivo using appropriate viral vectors that will be apparent to those of skill in the art.

In further embodiments of the invention, cells that are genetically engineered to
express the polypeptides of the invention, or alternatively, that are genetically engineered
not to express the polypeptides of the invention (e. g., knockouts) are administered to a

10   patient *in vivo*. Such cells may be obtained from the patient (I. e., animal, including
human) or an MHC compatible donor and can include, but are not limited to fibroblasts,
bone marrow cells, blood cells (e. g., lymphocytes), adipocytes, muscle cells, endothelial
cells etc. The cells are genetically engineered *in vitro* using recombinant DNA techniques
to introduce the coding sequence of polypeptides of the invention into the cells, or

15   alternatively, to disrupt the coding sequence and/or endogenous regulatory sequence
associated with the polypeptides of the invention, e. g., by transduction (using viral
vectors, and preferably vectors that integrate the transgene into the cell genome) or
transfection procedures, including, but not limited to, the use of plasmids, cosmids,
YACs, naked DNA, electroporation, liposomes, etc.

20   The coding sequence of the polypeptides of the invention can be placed under the
control of a strong constitutive or inducible promoter or promoter/enhancer to achieve
expression, and preferably secretion, of the polypeptides of the invention. The engineered
cells which express and preferably secrete the polypeptides of the invention can be
introduced into the patient systemically, e. g., in the circulation, or intraperitoneally.

25   Alternatively, the cells can be incorporated into a matrix and implanted in the
body, e. g., genetically engineered fibroblasts can be implanted as part of a skin graft;
genetically engineered endothelial cells can be implanted as part of a lymphatic or
vascular graft. (See, for example, Anderson et al. U. S. Patent 5,399,349; and Mulligan &
Wilson, U. S. Patent 5,460,959 each of which is incorporated by reference herein in its

30   entirety).

When the cells to be administered are non-autologous or non-MHC compatible
cells, they can be administered using well known techniques which prevent the

development of a host immune response against the introduced cells. For example, the cells may be introduced in an encapsulated form which, while allowing for an exchange of components with the immediate extracellular environment, does not allow the introduced cells to be recognized by the host immune system.

5   Transgenic and "knock-out" animals of the invention have uses which include, but are not limited to, animal model systems useful in elaborating the biological function of polypeptides of the present invention, studying conditions and/or disorders associated with aberrant expression, and in screening for compounds effective in ameliorating such conditions and/or disorders.

10   All patents, patent publications, and other published references mentioned herein are hereby incorporated by reference in their entireties as if each had been individually and specifically incorporated by reference herein. While preferred illustrative embodiments of the present invention are described, one skilled in the art will appreciate that the present invention can be practiced by other than the described embodiments, 15   which are presented for purposes of illustration only and not by way of limitation. The present invention is limited only by the claims that follow.

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CLAIMS

We claim:

1. An isolated nucleic acid molecule comprising

(a)   a nucleic acid molecule comprising a nucleic acid sequence that encodes
an amino acid sequence of SEQ ID NO: 30 through 55;

(b)   a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID
NO: 1 through 29;

(c)   a nucleic acid molecule that selectively hybridizes to the nucleic acid
molecule of (a) or (b); or

(d) a nucleic acid molecule having at least 60% sequence identity to the nucleic
acid molecule of (a) or (b).

2. The nucleic acid molecule according to claim 1, wherein the nucleic acid
molecule is a cDNA.

3. The nucleic acid molecule according to claim 1, wherein the nucleic acid
molecule is genomic DNA.

4. The nucleic acid molecule according to claim 1, wherein the nucleic acid
molecule is a mammalian nucleic acid molecule.

5. The nucleic acid molecule according to claim 4, wherein the nucleic acid
molecule is a human nucleic acid molecule.

6.   A method for determining the presence of a lung specific nucleic acid
(LSNA) in a sample, comprising the steps of:

(a)   contacting the sample with the nucleic acid molecule according to claim 1
under conditions in which the nucleic acid molecule will selectively hybridize to a lung
specific nucleic acid; and

(b)   detecting hybridization of the nucleic acid molecule to a LSNA in the
sample, wherein the detection of the hybridization indicates the presence of a LSNA in
the sample.

7. A vector comprising the nucleic acid molecule of claim 1.

8. A host cell comprising the vector according to claim 7.

5

9. A method for producing a polypeptide encoded by the nucleic acid molecule according to claim 1, comprising the steps of (a) providing a host cell comprising the nucleic acid molecule operably linked to one or more expression control sequences, and (b) incubating the host cell under conditions in which the polypeptide is produced.

10

10. A polypeptide encoded by the nucleic acid molecule according to claim 1.

11. An isolated polypeptide selected from the group consisting of:

(a) a polypeptide comprising an amino acid sequence with at least 60%

15 sequence identity to of SEQ ID NO: 30 through 55; or

(b) a polypeptide comprising an amino acid sequence encoded by a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NO: 1 through 29.

12. An antibody or fragment thereof that specifically binds to the polypeptide

20 according to claim 11.

13. A method for determining the presence of a lung specific protein in a sample, comprising the steps of:

(a) contacting the sample with the antibody according to claim 12 under

25 conditions in which the antibody will selectively bind to the lung specific protein; and

(b) detecting binding of the antibody to a lung specific protein in the sample, wherein the detection of binding indicates the presence of a lung specific protein in the sample.

30 14. A method for diagnosing and monitoring the presence and metastases of lung cancer in a patient, comprising the steps of:

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(a)   determining an amount of the nucleic acid molecule of claim 1 or a
polypeptide of claim 6 in a sample of a patient; and

(b)   comparing the amount of the determined nucleic acid molecule or the
polypeptide in the sample of the patient to the amount of the lung specific marker in a

5   normal control; wherein a difference in the amount of the nucleic acid molecule or the
polypeptide in the sample compared to the amount of the nucleic acid molecule or the
polypeptide in the normal control is associated with the presence of lung cancer.

15.   A kit for detecting a risk of cancer or presence of cancer in a patient, said

10   kit comprising a means for determining the presence the nucleic acid molecule of claim 1
or a polypeptide of claim 6 in a sample of a patient.

16. A method of treating a patient with lung cancer, comprising the step of
administering a composition according to claim 12 to a patient in need thereof, wherein

15   said administration induces an immune response against the lung cancer cell expressing
the nucleic acid molecule or polypeptide.

17. A vaccine comprising the polypeptide or the nucleic acid encoding the
polypeptide of claim 11.

20

1

SEQUENCE LISTING

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      Sun, Yongming
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acaccaaccc ccaaacaaga ccagaaggac gagccgcgag gtacagacag acaacgaaga    1500

caacgcacaa cacaacaaca caaacaccag cgtcgtcggt ctggggccac gaccacacca    1560
```

9

```
ggtcggtgca cacaacaagg gacagtcacc accccggagt gtgtgagata acaagttgta   1620

gtcttccgcc gcgctcaacn accaacagca tgacacggga ggacaggcac gatagaccac   1680

gacacaacaa cactgtccgc tggcgcagct agcaagccga caccgagccg cggcacgcag   1740

caagagccag cggtgcaccc acgccgcggc acgagccaac gacagcat                1788
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<210>   11
<211>   2467
<212>   DNA
<213>   Homo sapien

<220>
<221>   misc_feature
<222>   (2319)..(2319)
<223>   a, c, g or t


<400>   11
ggctctcatt gttctggggc ttgtcctcct ttctgttacg gtccaggcaa ggtctttgaa     60

aggtgtgagt tggccagaac tctgaaaaga ttgggaatgg atggctacag gggaatcagc    120

ctagcaaact ggatgtgttt ggccaaatgg gagagtggtt acaacacacg agctacaaac    180

tacaatgctg gagacagaag cactgattat gggatatttc agatcaatag ccgctactgg    240

tgtaatgatg gcaaaacccc aggagcagtt aatgcctgtc atttatcctg cagtgctttg    300

ctgcaagata acatcgctga tgctgtagct tgtgcaaaga gggttgtccg tgatccacaa    360

ggcattagag catgggtggc atggagaaat cgttgtcaaa acagagatgt ccgtcagtat    420

gttcaaggtt gtggagtgta actccagaat tttccttctt cagctcattt tgtctctctc    480

acattaaggg agtaggaatt aagtgaaagg tcacactacc attatttccc cttcaaacaa    540

ataatatttt tacagaagca ggagcaaaat atggcctttc ttctaagaga tataatgttc    600

actaatgtgg ttattttata ttaagcctac aacatttttc agtttgcaaa tagaactaat    660

actggtgaaa atttacctaa aaacttgggt ttatcaacat tacatctcca ggtacattcc    720

gtcttttttt ttggaaacgg agtctcgctc tgtcgcccag tgctggattg caggtggccg    780

caatctcttc gggatcactt gaaacctctc cacctctccc gggtttcacc gccatttctt    840

cctggcctca gcctctcccg agatagcgtg gagattatac gggtgccgcc ctgccaacaa    900

ggcccgggta taattttttc ggattatttt atagtatagg aagaacgagg ggttttccaa    960

ccaggtgttt gaccccgagg agagtgtgct ctctcgaact ctctcgcgtg acaccttgtt   1020

ggtgaactcc aacccacacc tctgcgtgcc tctccccaca agagtgtgcc gtggcgatat   1080

tcacgagggg cgtgtggagc ccacattttg gtccccgcgg tccaacatct ctacgcggct   1140
```

```
tctcatatat ctccaacgag aaaatataac cgcgacaaag acctataatc tcgtgtgaaa   1200

atgtgtatat cgcagcatat atatgtgccc ccacatatat ttatagaggt ataaaaacaa   1260

catttattag aagaaaaaaa ctgtggtttc actctcttat agacatatta cgatctctat   1320

gtaggacgca aaaatatata ccccagtgct gtgtagtgtg aagagggcga cattatctag   1380

tgagtgtggg cacattttac aaactctgtg ggtcacaggg cgcaatctcc tctcacagaa   1440

gacaacccgg ggtggaaaaa agaattaacc gccccactct ttctctgtgt gtgtgggcgc   1500

ggcggccaca ctttattgcg aagatcattc ttctctaaaa cacaaggggg gaatgtaaga   1560

agactatacc aaccccaagt attgtgctat aacgcgaaca caccgtgagc attctgggcc   1620

cccttgagaa tttttgggga ggacgacaat tacgtcagag gaataatcct cctcatacac   1680

aaaggctgtt gtggtggtgg tcgtctaccc ccttattcta ctactaataa caagcggtcg   1740

ccgcgggtgg acttcccccc ccaatcataa gcgagttctg cggggagcat acaacacgct   1800

atagcagacg agatcccacc aggtggtgat actatatcaa gtgcgaaatt ctaaaccaac   1860

tttcttttgg aagggaccca gaacatatta gagaacgccc tatttcaacc agagagtgta   1920

ttatagtttg ggcagcagca acatagtgta cacaccagaa acatttaagt acctcacgcc   1980

ccaaaatccg ttgtttttagc aacagcgttc ttaactgtgc cccctctttg atcgctgtga   2040

tacaccagac cacaatctct cccacaaaga ccaattttcc ctgacaatca taaacagagg   2100

gcgggctttt tggtggcgca caccaacccc caaacaagac cagaaggacg agccgcgagg   2160

tacagacaga caacgaagac aacgcacaac acaacaacac aaacaccagc gtcgtcggtc   2220

tggggccacg accacaccag gtcggtgcac acaacaaggg acagtcacca ccccggagtg   2280

tgtgagataa caagttgtag tcttccgccg cgctcaacna ccaacagcat gacacgggag   2340

gacaggcacg atagaccacg acacaacaac actgtccgct ggcgcagcta gcaagccgac   2400

accgagccgc ggcacgcagc aagagccagc ggtgcaccca cgccgcggca cgagccaacg   2460

acagcat                                                            2467
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<210>  12
<211>  251
<212>  DNA
<213>  Homo sapien

<400>  12
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ccactctgaa taactaatac cagagagagc tgcggggtgg ataagaaggc tgctgagtgt    120

ttccacgcct caccgctgct ggctgatgag gaaagagtca gcagatgtgg gttacaatgg    180
```

11

```
gattcttgca cgtttgtggt gccaatggat tctccacccc accacttcac cctgtaaggc     240

aaagctatga a                                                          251
```

<210> 13
<211> 624
<212> DNA
<213> Homo sapien

<400> 13
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cgcggccgag gtactcttga atacaagttt ctgataccac tgcactgtct gagaatttcc      60

aaaactttaa tgaactaact gacagcttca tgaaactgtc caccaagatc aagcagagaa     120

aataattaat ttcatgggac taaatgaact aatgaggata atattttcat aattttttat     180

ttgaaatttt gctgattctt taaatgtctt gtttcccaga tttcaggaaa cttttttttc     240

ttttaagcta tccacagctt acagcaattt gataaaatat acttttgtga acaaaaattg     300

agacatttac attttctccc tatgtggtcg ctccagactt gggaaactat tcatgaatat     360

ttatattgta tggtaatata gttattgcac aagttcaata aaaatctgct cttttgtatt     420

aaccggaaaa aaaacacaac aaaaaacaaa aaaaggcgc tgggggtacc ctgggccaaa     480

agctggttcc ctcggtgtgg aaattttgtt tcccggctcc cattcccccc aattctccgt     540

gacaaaccac aatgtaaaca caaaacacac aacaccaaac ccaaacacac accagacacc     600

aaaacaacac acacaagcaa acaa                                            624
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<210> 14
<211> 1623
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (856)..(856)
<223> a, c, g or t

<400> 14
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gcacgagcca ggccaataac tcagccagtg gcacagcagg actacagtca agacaatcac      60

agtctctgcg gacgtgccca agccctccat ctccagcaac aactccaaac ccgtggagga     120

caaggatgct gtggccttca cctgtgaacc tgaggctcag aacacaacct acctgtggtg     180

ggtaaatggt cagagcctcc cagtcagtcc caggctgcag ctgtccaatg caacaggac     240

cctcactcta ttcaatgtca caagaaatga cgcaagagcc tatgtatgtg gaatccagaa     300

ctcagtgagt gcaaaccgca gtgacccagt cacctggatg tcctctatgg ccggacacc     360
```

12

```
cccatcattt cccccccaga ctcgtcttac ctttcgggag cgaacctcaa cctctcctgc    420

cactcggcct ctaacccatc cccgcagtat tcttggcgta tcaatgggat accgcagcaa    480

cacacacaag ttctctttat cgccaaaatc acgccaaata ataacgggac ctatgcctgt    540

tttgtctcta acttggctac tggccgcaat aattccatag tcaagagcat cacagtctct    600

gcatctagaa cttctcctgg tctctcagct ggggccactg tcggcatcat gattggagtg    660

ctggttgggg ttgctctgat atagcagccc tggtgtagtt tcttcatttc aggaagactg    720

acagttgttt tgcttcttcc ttaaagcatt tgcaacagct acagtctaaa attgcttctt    780

taccaaggat atttacagaa aagactctga ccagagatcg agaccatcct agccaacatc    840

gtgaaaccca tctctnactg tagtcccagt tactcgggag gctgaggcag gagaatcgct    900

tgaacccggg aggtggagat tgcagtgagc ccagatcgca ccactgcact ccagtctggc    960

aacagagcaa gactccatct caaaaagaaa agaaaagaag actctgacct gtactcttga   1020

atacaagttt ctgataccac tgcactgtct gagaatttcc aaaactttaa tgaactaact   1080

gacagcttca tgaaactgtc caccaagatc aagcagagaa ataattaat ttcatgggac   1140

taaatgaact aatgaggata atattttcat aattttttat ttgaaatttt gctgattctt   1200

taaatgtctt gtttcccaga tttcaggaaa cttttttttc ttttaagcta tccacagctt   1260

acagcaattt gataaaatat acttttgtga acaaaaattg agacatttac attttctccc   1320

tatgtggtcg ctccagactt gggaaactat tcatgaatat ttatattgta tggtaatata   1380

gttattgcac aagttcaata aaaatctgct cttttgtata acaaaaaaaa aaaaaaaaaa   1440

aaaaacaaaa aaaaggcgct gggggtaccc tgggccaaaa gctggttccc tcggtgtgga   1500

aattttgttt cccggctccc attccccca attctccgtg acaaaccaca atgtaaacac   1560

aaaacacaca acaccaaacc caaacacaca ccagacacca aaacaacaca cacaagcaaa   1620

caa                                       .                        1623
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```
<210>   15
<211>   393
<212>   DNA
<213>   Homo sapien

<400>   15
cgatgatcac tacatgggca atggtgctct agatgcatgc tcgagcggcg cagtgtgatg     60

gatttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttcctgaat    120

cccttttttt cccccccggg ggggggggtg gtggggagca gtaaacatca ggcccaggaa    180

gagttgggtt gcgtcccgtt cttggccatt gtgcctcctc tggaaaataa cacttcaacg    240
```

13

```
atatttcacc tccctcataa ggctggtggg tgtacctcag tggctcatat agtcgtgatt      300

cccgtggtgt gtaaaagtgg tttactccgg cacccaattc tcccacaaaa cattagcaaa      360

aaactgcatg aacataacac accggtaaca aga                                    393
```

```
<210>  16
<211>  839
<212>  DNA
<213>  Homo sapien

<400>  16
taatgcatgc tcgacgcggc gccattgtga tggatgtcga cgtaatcctc tgcagtgata       60

cttctggtaa atgtcaccca gagtctttac gttcaggtca aatgttcctg tatatgttta      120

ttgcaaatag agctgtatac tgttctaaat gtacgacagg tgaactgaac tggcggttat      180

gctcaccatg cgagcacggt aaagggcaga acttcttaac aatgccaata cactgcatat      240

acacaggtgc gtttgttgtg cagttgacga gtaagtacca tgtgacgcga tagatctcta      300

ctatttgacc acggtgtgac gtcccacagc ataggtagga catgtgtggg caagcgttca      360

atgcttgcaa ggaccgcaca tcgtcacatt ggagtggaac actagcaacg ctcatagcta      420

cttataacaa gcgcagtgcg taaactattt caagtgacat acgcatggat aggtctctaa      480

tagatggtcg aacacaactt tgtaaaactc acgtcgaaga tccgcgagct gcccatttta      540

taggggggaa tgccgaatgc tggggccctt gctaattacc caaaacactt tgcttaaaca      600

cttccaagct tttatccatc gttgcacact gcccttaggt gctcggtta catcttccat      660

cttgcggttc ctacttaacg gcccttaggc atatttattc ccccatttgg tttggctttt      720

gaacaacaaa ccttgttggg cttctaagtt tttccccgag gggcttttcc caaaccaaat      780

aattttatcc acctaaccta acctaaaaat cccaataacc cgcgtgaaaa tggcccaat       839
```

```
<210>  17
<211>  1176
<212>  DNA
<213>  Homo sapien

<400>  17
cgtggtcgcg gccgaggtct tttttttttt tttttttttt tttttgggga cacaaaccca       60

cttttattac agatttgacc cagcccaaca cgcgcggggc agggtcaaac ctcacaagac      120

atctccgcac caaggggccg gggagacctc aagaaggggc tagaaagggc ttcactctgg      180

agaaatgggg ccccggctct cacaacgccc gggtataccc ccaatactct caaacaacgt      240

gcgcgtgctc tctttatgtc tccccgcaat tgtggccaca ctcctgtgtc gccccgagtg      300

tgcgtggagt tctctcgtgg tcgcacttaa ttttttctct ctcaccacca cagagggtg       360
```

```
tgccgtggcg agcgcaacac tgtgggagcc tcagcgtggc ctcacagagc gctgggggcg    420

ataacactcg agtggcgcaa catatagcgc gtgtgtctcc gcgcggtggg gggacacatg    480

tgtgggtata tctcgcgggc tctcacacca aattctcccc cacaaacaaa acatatagcc    540

gggggacaac acaaaaaggg ggcaaaaaag aaaggggaga aaacaagcca ccagagagag    600

gagacgagca ccaaataata agatgaaaac ggaataggaa gaacaaaaaa caacactcca    660

caaacaatct aaactaatga tggggcgacg aaaagaagag cgcaccaaag ccacaacgat    720

gacaccgcag agagtatatc cccacaaaca cagacatccg gggagaaaac acaccccacg.   780

tatgtattag gagtcagcaa ccacacgacg agagtaaaca tataatcaga agtagagcaa    840

aactaactgg gaggcacaca aatagcagcc gcacgcacga aggtggaaaa agaaagcagc    900

gaggattata ttcaaggacg agtaaaacat aatggggaga gaaccacgca catctcatta    960

cccccgcatg gactatcacc cccatcgggc gcgtcgacag aacatatgaa aacaactcgc   1020

acccatagcg caggccacac cccccggca ggacccagcg acacacgcga ggagctataa    1080

gcgtgagaga cgaaacaaca ccggaagtaa agatacgaag cgatctcacc acaccacaga   1140

aaaaggaggc cgcgaatcgc aaaatacaca acgggt                             1176
```

```
<210>  18
<211>  1069
<212>  DNA
<213>  Homo sapien

<400>  18
cggccgcccg ggcgggtacg tgccgcgtaa aatgctccgc gtaatcaatc gcatcatcgg     60

tgccaggtaa ccacgcatcc actccagagt gaacggtggc cagaggttgg acaacggtca    120

catgtgcccg tgtttagtct gcgccacgtt tagaatactt gatggctatc tgagcgtggg    180

actacttcga gtacgtgaat ggagtagagc tcaagactcg tattccagtt actcctgatt    240

cggccagatg gctcgccttg gctatcagat ctcagataag acactgcttc tgacatggca    300

cgacgacaat cacatagata gtcgagaact attctgtcca taaactaaac taagtgagaa    360

actatacaaa aaacaaacaa agaacaaaga caaataacaa cagagctctg aggcgagagt    420

accactgagt gggcgcaaaa atgaacggta gtgtcccccc ggtggtgtgc gacacacact    480

gtgtgtatca ctcccgcgac ctacacacat gaaatctccc ccacacagac acatatatac    540

ccggaaaaat ccacaaacga gttaaaacaa tctcaagact aggccaagtt ccgtcaacca    600

tttgccggat cacggtccca ccatctctct caccacacag gctgacatgc ctacgtcacg    660

agacatctca acgcgcagcg caaacaccta cccacacgtt ctcccggtcc tcacgttgta    720
```

```
atcacgactt ccacgaacaa ctgcgatacc gaaacacagt actcgggccg gatcccgtcg      780

tatgagcccc caaccactcc aacatattgt accactcttg cacacgcaac catcccacat      840

atcaacaaaa actagaagac atattacgat tatctatcct gtccccatac tatacttccc      900

acaaagtcgg cgaagaaata gagacgacgc tcgcattggc tttactatcc cctataaacc      960

ctacctttga agttgatacc gaggagcaca caacacagat ttacaccgcc ctggcaacca     1020

tgcactggga attcactggt acatacaaca acactctatg cgccagtca               1069
```

```
<210>  19
<211>  637
<212>  DNA
<213>  Homo sapien

<400>  19
attatccaga acagaggaaa acactgatcg tgccagcctg acattcaata gaatacggcc       60

aacagcgacg ggacagaggc agaatagaca gtaatagagc gacggcctct tatccgacct      120

atcctcagat cacgtgagcc atacagacat gcagcatcag agtcgtagac gagctagcgg      180

cacgagcgag atatacagac tacacatcaa agagacggta gatacggtag ataccacgag      240

aatcacggga gaataacagc acggacaagc aacatgtaga gacgaaagag gccagacaaa      300

aagcgccagg aaccgcgaaa aaggccgacg ttaggtggcg tagaaccata acgacacacg      360

aacaacactg acagaacata cacaaaaatc agagcatcaa gtcaaagtag gcgaaaccac      420

gaaagaccta ctaaaaattg cgaggggtt tcccgcgttg gcgcatcaca tcgtagggat       480

cataatgata ccggacatga cgatatacac ggataacttg tacggcttat acgcttgggg      540

aaggatgaag gtacgcatag ctcagcagga ggatccacac caggaacgaa gaaggcaaac      600

tggctgtgac aaacaccgga accggaagaa caaacga                              637
```

```
<210>  20
<211>  895
<212>  DNA
<213>  Homo sapien

<220>
<221>  misc_feature
<222>  (365)..(365)
<223>  a, c, g or t


<400>  20
gtccgcggcc gaggtaccat cagccagcac cacccactat ggcctcagct cggatggccc       60

cagtacccca ccgctagcga cccagcggga tgagtttgcg tgtagctatg ctgagactta      120
```

16

```
acgtggttgg cttcagcgtg ggtcgggctc gcatcttacg atggagtaga tgtccagttc     180

aagaggccaa ctgactcatt gcatgccaga gggaggtgtg gatacgtcgg cgcgatcaag     240

aatgccgcac tcatgcgacg ctgacgccct tgcttggtcc gtgggtgatc aggcagcagg     300

tagagtctga gccactcaga gcttgggcga taatcactgg atcactaggc tgtattctct     360

ggtgntcgaa agtctggtta ttcctggctg ctagcgaatt cctatcatca agcataccgg     420

agtcacgggc gctcgatcat ggcctgaatg caggggaggg tgctttagag cgcgtgctgc     480

cgagtcgaga gtgaagatgc ctgagtcaaa tgggccaaga agtgacagac aaactcgggt     540

tcgggcagtt attcgcagtg cggtcgaagg gggccggcat gtgcaatacg atgctgatca     600

gattgatgcg aataactgga gtaagtgcag tacgacaaag ggcgctctca gagcaagaag     660

acattgccgc ttagtgtaga gtgtagccta ccttgtactt cgacattggt caacggccag     720

aaggacatgt gaaacactag ttgtgggaga cgacctgtgg ggaccggatt cacgtgccaa     780

tgggcttcag taagacgtgg gtatttccca tgggtgcgct gcaacaaata gggtcaagtg     840

cccagactac gaagcaattt cccaccaagc aaatataggg ggaagccaag ggggt          895
```

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<210>  21
<211>  506
<212>  DNA
<213>  Homo sapien

<220>
<221>  misc_feature
<222>  (276)..(276)
<223>  a, c, g or t


<220>
<221>  misc_feature
<222>  (462)..(462)
<223>  a, c, g or t


<400>  21
cgcttaggca ggtactcacc ccccaggata gagaagtgtt gttagggaga gaagagggag     60

aggcaggagc gcggcccaag cccaggtccc tgctgggccc cagaaagcac ttaaccaggc     120

cccaagcctt caagggaaac caaggcctca accagacaat cttgagggaa ggaaaagcca     180

gactttggcg ttgttttttg ggggaattat tggttttttt ttatgtttct tttggaattt     240

tgtttgttgg ccaaattccc tgtgtgatct tttttncata aaacaacaaa gcaaaagatt     300

ataatccgga aaacaggaaa acaaagaaag aaacaaaaaa caacaaacaa aaggtctggg     360

ggtgacctct gtgggctcat aaggcgtggt tcccgggtgg tggacattgg gtgttcccgg     420
```

```
cgtcaacaat tccccaaaca acaaacacgg gcacgacaag tnggggcaca acgcctggag    480

cccgtgagcg gacaaggaga cggaaa                                         506
```

```
<210> 22
<211> 5387
<212> DNA
<213> Homo sapien
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<400> 22
cgcctggcac tctcacccga agacaagccc atccgcttgt ccccctccaa gatcacagag    60

ccgctgcggg agggcccgga ggaagaaccg ctggctgagc gggaggtgaa ggcagaggtg    120

gaggacatgg acgagggccc cacagagctg ccgcctctgg agtcgccgct gccactgccc    180

gccgcggaag ccatggctac ccccagccct gcaggggtt gtggaggtgg cctgttggag    240

gcccaggcgc tgagtgccac cgggcagagc tgcgcagagc cctctgagtg tccagacttt    300

gtggagggc ctgaaccacg ggtggattcc ccgggccgga cagaaccctg caccgccgcc    360

ctggacctgg gggtgcagct gacacccgag acactggtgg aggccaagga ggagccggtg    420

gaggtgcctg tggggggtgcc cgtggtggag gcagtgcccg aggaaggcct ggcgcaggtg    480

gcaccgagcg agtcccagcc caccctagaa atgtcagact gtgacgtgcc cgccggggag    540

ggacagtgcc cgagcctgga gccccaagag gccgtgcctg tactcggcag cacctgcttc    600

ctggaagagg caagctctga ccagttcctg cccagtctgg aggacccact ggctggcatg    660

aacgccctgg cggcagctgc ggagctgccc caggccaggc ctctgccctc cccgggtgct    720

gctggagccc aggccttgga gaagctggaa gcagccgaga gccttgtctt ggagcagagc    780

ttcctgcatg gcatcaccct gctaagtgag atcgcagagc tggagctgga gaggaggagc    840

caagagatgg gaggtgcgga gcgggccctg gtggcgcggc cctccctgga gagtctgctg    900

gcagctggca gccacatgct gagggaggtg ctggatgggc ccgtggtgga cccactcaag    960

aacctgcggc tcccgcggga gctgaagccc aacaagaagt acagctggat gcgcaagaag    1020

gaggagcgga tgtatgccat gaagtcctcc ctggaggaca tggacgccct ggagctggac    1080

ttccggatgc ggctggccga ggtgcagcgc cagtacaagg agaagcagcg tgagctggtg    1140

aagctgcagc gccgccggga ctccgaggac aggcgcgagg aaccccatag aagcttggca    1200

cgcagaggcc ctggcaggcc gcggaaacgg acccacgccc cgagcgccct gtcgcccccc    1260

cgcaagagag ggaagagcgg ccacagtagc ggaaagctga gcagcaagtc tctgctgaca    1320

tcagatgatt atgagctggg agcagggata agaaagagac acaaggggtc tgaggaggaa    1380

catgatgccc tcatcggaat ggggaaagcc aggggggagga accagacttg ggatgaacat    1440
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18

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gaggcctcgt cggacttcat cagtcagcta aagattaaga agaagaagat ggccagcgac   1500

caggagcagt tggcaagcaa gctcgacaag ccctctccc  tcaccaagca ggacaagttg   1560

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aaggacgagt ggcccgccca aggcccctcc agctccaaac tgacgccttc cctcctgtgt   1920

agcatggtgg caaagaacag caaggcagct ggtggcccca agctgaccaa gagggggcctg   1980

gcggcccccc ggactctgaa acccaagccg gccaccagca ggaagcagcc gttttgtctg   2040

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agtgggctgg gcctgctggc acgcttcgcc gccagcgccc tccccagccc cacggtgggt   2280

ccatccctgt ctgtggtaca gctggaggcc aagcagaagg cccggaagaa agaggagcgg   2340

cagagcctgc tgggcacaga gttcgagtac accgactcag agagcgaggt caaggtgcgc   2400

aagcggtcgc ctgcggggct gctgcggccc aagaaggggc tgggggagcc gggaccctcc   2460

ctggccgcac ccacgcctgg cgcccgcggt cccgacccca gcagcccaga caaggccaag   2520

ctggcggtgg agaaggggcg caaggcccgg aagctgcggg gccccaagga gcctggcttc   2580

gaggcggggc ccgaggccag cgacgacgac ctgtggacgc ggcgccgcag cgagcgcatc   2640

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aggccggcaa ggcgcggccc tcggcccact ccccaggcaa gaagacgccc gcgccccagc   3180

cccaggcgcc tcctccgcag cccacacagc ctctgcagcc caaggctcag gccggggcca   3240
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agagccgacc caagaagaga gagggcgtcc acctccccac caccaaggag ctggccaagc   3300

ggcagcgcct gccgtccgtg gagaaccggc ccaagatcgc cgccttcctg ccagcccggc   3360

agctctggaa gtggttcggc aagcccaccc agcggcgtgg catgaagggc aaggcccgca   3420

agctcttcta caaggccatc gtgcgcggca aggagatgat ccgtatcggg gactgtgccg   3480

tgttcctctc tgccggccgc cccaacctgc cctacatcgg ccgcatccag agcatgtggg   3540

agtcgtgggg caacaacatg gtggtccgcg tcaagtggtt ctaccacccc gaggagacca   3600

gcccgggcaa gcagttccac cagggccagc actgggacca gaagtccagc cgcagcctcc   3660

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tgctctgctg agcccgccgg gccctgcggg ccacctgtgc cccgagggcg gccagggacc   3960

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caggcgtgtg catggggcca ggtgtgcacg tggatgcccg ggtgagtgtg tgtgcatgca   4080

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tgtctgtcaa aggcaccagg tggagagggc ccggcacagg cccaccctgg tccaaaccct   4560

cacactacag aaaaccccaa tggtgctgaa actgtcgccc ggccacgcct ggcccctccc   4620

cacccaggag ggaggtggca cttcttaacc tgtacagttt tattgtacca agagactcgc   4680

cccgcccctg tatcataagc ctttaaatgg agtcaacttt ttaattatat atataaagat   4740

aaatatatat aaatatatat ataaactttt taaaactgtg aaaaatagct atgaaattat   4800

aaaaaaaaaa cattctgacg tgcagaatat tatttttat ttcctgttag attatagtgt   4860

ctagcaccgg cttcaccggc ctcccagtcc ccagcacacc ccccgcccac cccgccaagt   4920

gtactgtact cacccccag gatagagaag tgtttgttag ggagagaaga gggagaggca   4980
```

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ggagccggcc caagcccagg gtccctgctt gggccccaga aagcacttaa ccaggcccca   5040

agccttcaag ggaaaccaag gcctcaacca gacaatcttg agggaaggaa aagccagact   5100

ttgggtttgt tttttggggg aattattggt tttttttttt atgtttcttt tggaattttg   5160

tttgttggca aattctgtgt gatctttttt cataaaaaaa aagaaaagat ttaattggaa   5220

aaataaaatt gtctggagtg gtttatttca ggggctggag tagggtggt  gtctgggggc   5280

attctgccat atcagggcac caagaagcag gattcgactg gaagaagttg ggtgccacgc   5340

gtgcaggggc ggtgacccca tgcagccatc taaatgagct catcggc              5387
```

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<210> 23
<211> 361
<212> DNA
<213> Homo sapien

<400> 23
tcatataggg cgcatggtca tctagatcat gctcgagcgg cgcattgtga tggatggtcg    60

cggccgaggt ccggccgagg tacatttatt taggagtggg tttcgtgggg gtaggtgata   120

aaaattagga tcagttgaag aaaattgaag aaactaggat cagtaagaga aactgtttgc   180

tttacctgaa tttaactatg aaaacacact taacaatctt acacgtttct agatattaag   240

tgaatatgta actcctgtcc atgggtagat gtgtatcttt gacttctgta attattttttg   300

atattctatc agtgtattat gagactctgg cctccctgca gatcttctaa gaaccacact   360

a                                                                  361
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<210> 24
<211> 1682
<212> DNA
<213> Homo sapien

<400> 24
gtggcaattc ccccacttac acacaatctt tctgcagttg ctcccagcat taattctgga    60

atggggactg agactatacc aattcagggt tacagagtgg atgagaaaac taagaagtgt   120

tctattccat ttgttaaacc gaacagacat tccccatcag gcatttataa cattaatgtg   180

accacattag tctctagtga aaaaaacctc tttgggcaag taagaaaaga agagaatact   240

ccaggacaga tgtccgtttg cctgaactaa actataatca tctccctgaa ctaagagcac   300

tgggaggcat agctcgaaat tccaggctaa caaagaaaga gagcaaaatt ctttcagaat   360

ctcgaattcc ttctctggct gctattgacc tgcacacccc cagtattaca ttacatcagg   420

tatcaggacc tcccctgtca gatgattcag gggctgattt gcctcaaatg gaacaccagc   480

actgagaacc attttggttc tgaactggat gatgctcttg cacttgagat gacatcttct   540
```

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tgcagcaaga gtgctgatat cccaagagga gagattcatg gttttgatca tttccttctg    600

aactgcctgc attttctgag gaaggccttc tagaagaagg aaagacaaag acttccaaat    660

gtttcaaagg aagattgaac aaatggccct ccccaactgt tatcccatta cctttcacgt    720

ccaccgatgc tatttcaaga catatccagt ggaataacag tgatatggtt cttgttacat    780

gaatgtgtat ttactgttag gagattgtat attttaagtt accatgatta aaagtgtgta    840

aaaaggggg acagagagaa atactataaa aggccatgtt actcatgcat tgaactttgt    900

gtgttttctg tataaatgtg tacatttatt taggagtggg tttcgtgggg gtaggtgata    960

aaaattagga tcagttgaag aaaattgaag aaactaggat cagtaagaga aactgtttgc   1020

tttacctgaa tttaactatg aaaacacact taacaatctt acacgtttct agatattaag   1080

tgaatatgta actcctgtcc atgggtagat gtgtatcttt gacttctgta attatttttg   1140

atattctatc agtgtattat gagactctgg cctccctgca gatcttctaa gaaccacact   1200

aatgcaagct tgacagagaa acctcttcg aatgacttac tacaactctg gcattggtta   1260

gttccatgta ttgtaagatt ctggtgctaa tgctccatac agaattgatc aggactgatt   1320

actcttctgt ggaccaattg ctattgaact acccagctga gagggtttg gggagagaac   1380

gttcattatt atggactcca cttttgtccc ctggtagttt aagggtgata ctagaatcca   1440

gagaagttcc tgtctccttg tggcctcaaa cactcaggcc gtctcaaaag cttttcacca   1500

aggtgcaaaa tcatttacct gcattccaca catcttttcc aatgcatgga tccaaaactt   1560

tttaggtggg aggaataaac taagttggct acaggttctt gatttctggg tttctacaca   1620

tgctctgcat ttatcatttt agagaatggt tgtttaggga accagaattt gtgagttttt   1680

tt                                                                  1682


<210>  25
<211>  718
<212>  DNA
<213>  Homo sapien

<400>  25
cggccgaggt accagagaac atacagtaaa taatgatttt tacatattga agttgcagtt     60

gttgactgtg atgttgaaga tgtcttcaga cagtagttca tactgcattc cacacttgag    120

gctcaagtga ttggagtgat ttctgcaatt actagtttgt tctataacta agactgtttg    180

ttggtctctg catatacttt caggtcatta aatgctacag aaatgagaaa tgaaatacaa    240

acttttttaac tcctactcag atgtccaaac agcttcttag ttcctgtcag atcagtaata    300

atactgggtt tggtctttct taaaccaagc ataatcctgc ttatcttaga atgaaacagt    360
```

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attcctattc agaggtaaat agagttaacc tttactcgtg taattttttat tgttgttttta      420

ccatttcatg gtgttcatac tagccccctt tcctttccct ctaagtgact gctgaggttc      480

tcaccatttc agaataaaat tcttgtcctt tgaggttgga aatttaatga taatgaaaaa      540

ctgtatgtgt cagtatactt aaaaggaaag gttatatcat tctcctcatt tggatgtaaa      600

atttacctgt tagagaacac attggaatta tagaacagaa acacacccccc aaacacacgg      660

ctgggcgtaa ccagggccaa agcggcccgg ggtgaatggt atccgcccca aatccatc       718
```

```
<210>   26
<211>   708
<212>   DNA
<213>   Homo sapien

<400>   26
ggatacacag aatgatcata tatgggccat gttatctaga tgcatgctcg agccggcgct       60

aatgtgatgg atggtcgcgg cgaggtacca gacatgctca aaatgtgctt tcccgttatc      120

tttcagaacc caccaccagg aaaccaaaac ggaccccact ctgagagttc catgatgaag      180

gtgtttaatg aaatcacatt aaccccctaag taaaggcagt agatgaaatt atccattatc      240

ttttgtctct tttttttttca tagtgtgaga ctacgattgg caaagtggga aaacggacac      300

ccaactcatt tgattagcag aataaatggt gtccattaaa tccctcctct ttgaaagtta      360

tgtgcatggc ccagcagtgg tacgctttag tgccctgcaa ctcccagaca ctttcgggag      420

gccgatggca gaaaggactc gcttgagccc aggagtccga gcaccagcct gggcaactta      480

cgtagggacc ccatctcgtg gttttcttct tttgtacgaa aagaagcaga tttctgtggc      540

gaagacgcta ttgcagacca caagggaggc tcataggaac actgtctcat attgattact      600

ctatgagaag aaactcccgt gtatggaaag ggggcactga gagatctggg cgctcgagag      660

aaacagtggg ggacgcacag ggccggataa gatccaagcc cctattat                 708
```

```
<210>   27
<211>   1026
<212>   DNA
<213>   Homo sapien

<400>   27
ggtcaaagcg ggaaaccaaa gagtatgtgg tatccatatt cgttgcaaaa atgataatta       60

ctggaatttt ccaaacatca aasgaagggg gatcaatggt taccactatc gttttcagcc      120

aatatacaga tgttcgctca aggtctaggt tttatttcta catagtagta ttcacatgag      180

ttccctattc tgaagtatta tcaaaacgag gacccttgaa ggtcgagccc agcttgtctt      240
```

23

```
gacttcaaag atgacacagc agccaaccta gaatcctggc ttgctgcttg agtcctagaa    300

atcatgtctt ctcatgtttt acaacaagct gtgtctctga aaactaaaat cagacttcag    360

attcctctga aacagttctg gttcccaagc atccgcacca tggtacccag acatgctcaa    420

aatgtgcttt cccttatctt tcaaaaccca ccaccaggaa accaaaacgg accccactct    480

gagagttcca tgatgaaggt gtttaatgaa atcacattaa cccctaagta aaggcagtag    540

atgaaattat ccattatctt ttgtctcttt tttttttcata gtgtgagact acgattggca    600

aagtgggaaa acggacaccc aactcatttg attagcagaa taaatggtgt ccattaaatc    660

cctcctcttt gaaagttatg tgcatggccc agcagtggta cgctttagtg ccctgcaact    720

cccagacact ttcgggaggc cgatggcaga aaggactcgc ttgagcccag gagtccgagc    780

accagcctgg gcaacttacg tagggacccc atctcgtggt tttcttcttt tgtacgaaaa    840

gaagcagatt tctgtggcga agacgctatt gcagaccaca agggaggctc ataggaacac    900

tgtctcatat tgattactct atgagaagaa actcccgtgt atggaaaggg ggcactgaga    960

gatctgggcg ctcgagagaa acagtggggg acgcacaggg ccggataaga tccaagcccc   1020

tattat                                                            1026
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<210>   28
<211>   406
<212>   DNA
<213>   Homo sapien

<400>   28
gaagatgact catatagggc gatggttcaa catagatgca tgctcgagcg gcgcgttgtg     60

atggatgcgt ggtcgcggcc gaggtactcc acttcaaatt tcccaagaaa tcagaagaat    120

ggtgaacaag tgctggtttc acaatactca gcaagtgttt acacattggg ccaaggacag    180

attttttcctg gagaaggatt ttaccactgc caccatcttg aaattcttca tcgtttggaa    240

cacagagcca tagattttca tttctgcact cagctctgtt ctgagaccgg ggccataggg    300

gttcttggag agacagggca gatggaagaa gtggaaggca tctgcacact gtagagtgcc    360

tttaagccac ccccattgcc tgagttgttt tccttttttta caaatg                  406
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```
<210>   29
<211>   818
<212>   DNA
<213>   Homo sapien

<400>   29
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cttcaaattt cccaagaaat tcagaagaat tgtgaacaag ttgctggttt cacaatactc    120
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agcaagtgtt tacacattgg gccaaggaca gatttttcct ggagaaggat tttaccactg    180

ccaccatctt gaaattcttc atcgttttgg aacacagagc catagatttt catttctgca    240

ctcagctctg ttctgagacc ggggccatag gggttcttgg agagacaggg cagatggaag    300

aagtggaagg catctgcaca ctgtagagtg cctttaagcc accccattg cctgagttgt     360

tttcctttt  tacaaatgaa gcttgttctt ttctgggtct ctccaaggtg gagtgtagga    420

gggcagtgtt ttccgtagcc tctggctcgt gccgcgctct cagactcttc agttctcctc    480

acccacacga gcccaatgag gtaggccttt ttattccatc ttgcagacaa agaaacgatt    540

actcagggtt gataaacacc acccaagatc tcatgggagg aaggaacaga gatgaaaata    600

aaatgcaagg ctgtgtaagt ccaacaaata tgccacatcc atgtcacctc tggggtctga    660

tccagcctct caacaaccac cgtcacccct caacaggcag gtgacagtgg cgagacggcc    720

cagcccagca acaggctccc ccattgcagt gccattgcta tgccagagga cacaaacccc    780

agaccttgac tcctcctcac agaccctgaa cagctaga                            818
```

```
<210>  30
<211>  57
<212>  PRT
<213>  Homo sapien

<400>  30

Met Leu Trp Pro Arg Leu Ser Leu Ser Arg Thr Pro Pro Val His Leu
1               5                   10                  15


Ser Arg Cys Asp Thr Arg Arg Arg Arg Leu Ser Glu Pro Leu Pro Lys
            20                  25                  30


Ser Val Arg Gly Glu Ile His Arg Ala Cys Glu Arg His Thr Lys Cys
            35                  40                  45


Pro Val Ala Leu Ile His Tyr Ile Ile
        50                  55


<210>  31
<211>  80
<212>  PRT
<213>  Homo sapien

<400>  31

Met Ser Tyr Lys Asn Gln His Thr Lys Gln Thr Glu Gln Phe Arg Ser
1               5                   10                  15
```

Leu Cys Tyr Ser Leu Pro Asp Leu Arg Ser Tyr Cys Leu Ala Tyr Pro
          20   25   30

Pro Ser Thr Tyr Leu Cys Tyr Phe Leu Ser Asn Ile Gln His Ile Pro
          35   40   45

His Thr Asn Ile Thr Asn Arg Ser Thr Ser Gln Gln Arg Val Ile Tyr
      50   55   60

His Ser Ser Leu Thr Ala Leu Val Thr Ile Leu Asn His Pro Gln Thr
65   70   75   80

<210> 32
<211> 41
<212> PRT
<213> Homo sapien

<400> 32

Met Cys Val Thr Arg Ser Leu Leu Asn Cys Leu Tyr Arg Ile Pro Trp
1   5   10   15

Leu Glu Ser His Asp Cys Ser Phe Gly Ser Ala Pro Glu His Cys Thr
          20   25   30

Glu Thr Ala Cys Val Gln Gly Val Gly
          35   40

<210> 33
<211> 135
<212> PRT
<213> Homo sapien

<400> 33

Met Met Ser Ser Ser Ala Ser Pro Leu Ser Leu Pro Leu Ser Leu Trp
1   5   10   15

Arg Phe Ser Thr Leu Pro Ala Leu Pro Arg Ala Gln Phe Pro Pro Asp
          20   25   30

Pro Thr Lys Val Lys Gly Glu Glu Glu Lys Arg Gly Arg Gly Ser Asp
          35   40   45

Ala Thr Ser Val Leu His Leu Val Ala Glu Arg Glu Gly Pro Thr Arg
      50   55   60

26

Asp Arg Gly Ser Leu Cys Val Cys Val Cys Val Cys Val Cys Val Cys
65   70   75   80

Val Cys Val Cys Val Leu Arg Trp Ser Leu Ala Leu Ser Pro Arg Leu
           85   90   95

Glu Gly Ser Gly Ala Ile Leu Ala His Cys Asn Leu Arg Leu Pro Gly
           100   105   110

Ser Ser Asp Ser Pro Ala Ser Ala Ser Gln Val Thr Gly Ile Thr Gly
           115   120   125

Val Pro Arg Pro Arg Pro Arg
    130   135

<210>   34
<211>   90
<212>   PRT
<213>   Homo sapien

<400>   34

Leu Arg Trp Ser Leu Ala Leu Ser Pro Arg Leu Glu Cys Ser Gly Ala
1   5   10   15

Ile Leu Ala His Cys Asn Leu Cys Leu Pro Ser Ser Ser Asp Ser Pro
           20   25   30

Ala Ser Ala Ser Gln Val Ala Gly Ile Thr Gly Ala His His His Val
           35   40   45

Gln Leu Ile Phe Val Phe Leu Val Glu Thr Gly Phe Arg His Val Gly
    50   55   60

Ala Ala Ala Leu Glu Leu Leu Thr Ser Gly Asp Pro Pro Thr Ser Ala
65   70   75   80

Ser Gln Ser Ala Gly Ile Thr Gly Val Thr
               85   90

<210>   35
<211>   218
<212>   PRT
<213>   Homo sapien

<400>   35

Met Gly Val Pro Ile Leu Leu Asp Ala Arg Ser Ser Pro Thr Pro Thr

27

```
1              5              10                  15
```

Pro Ala Ala Ser Pro Arg Val Pro Val Val Tyr Asp Ser Leu Arg Pro
                20   25   30

Pro Arg Arg Pro Gly Pro Gln His Leu Pro Tyr Phe Val Pro Pro Pro
                35   40   45

Asn Phe Trp Gly Ala Pro Tyr Leu Leu Pro Ala Arg Pro Trp Pro Leu
                50   55   60

Phe Thr Ala Phe Gly Arg Ser Pro Ser Val Cys Pro Cys Ser Arg Ser
65   70   75   80

His Gly Cys Phe Ser Ser Pro Ala Pro Pro Thr Thr His Leu Phe
                85   90   95

Cys Pro Val Ser Cys Pro Gln Ala Pro Ser Gly Thr Pro Phe Arg Arg
                100   105   110

Glu Thr Leu Gly Asp Glu Cys Pro Pro Ala Thr Ser Met Pro Pro Ala
                115   120   125

Pro Cys Pro Ile Pro Glu Ile Phe Arg Gln Tyr Leu Lys Trp Val Pro
                130   135   140

Leu Met Asn Arg Gly Ile Pro Trp Gly Asn Pro Thr Arg Gly Ile Trp
145   150   155   160

Ala Pro Phe Gln Cys Gly Glu Lys Lys Lys Phe Trp Leu Cys Pro Pro
                165   170   175

Leu Asn His Lys Lys Lys Lys Lys Lys Lys Lys Ser Thr Ala Ala
                180   185   190

Ala Thr Thr Ile His His Thr Ala Pro Leu Glu His Ala Ser Arg Met
                195   200   205

Asn His Gly Pro Ile Cys Leu Ser Phe Ser
                210   215

<210> 36
<211> 61
<212> PRT
<213> Homo sapien

<400> 36

Met Thr Gly Ile Thr Leu Asn Ile Cys Arg His Leu Cys Asn Leu Ser
1   5   10   15

Arg Val Asn Leu Thr Phe Arg Asn Cys Val Phe His Ser Arg Met Val
            20   25   30

Met Ile Leu Gly Cys Asp Ile Trp Asp Leu Pro Thr Met Gly Thr Leu
        35   40   45

Asp Lys Met Asn Thr Asp Glu Pro Thr Asp Leu Cys Tyr
    50   55   60

<210> 37
<211> 56
<212> PRT
<213> Homo sapien

<400> 37

Met Ala His Cys Ser Leu Asn Leu Leu Gly Ser Ser Asn Pro Ser Val
1   5   10   15

Ser Val Pro Gln Val Thr Arg Thr Thr Gly Met Cys His His Trp Leu
            20   25   30

Phe Phe Cys Leu Phe Phe Glu Thr Thr Ser Tyr Tyr Val Ala Gln Ala
        35   40   45

His Leu Glu Ala Pro Gly Leu Lys
    50   55

<210> 38
<211> 96
<212> PRT
<213> Homo sapien

<400> 38

Phe Phe Phe Phe Phe Ala Gly Lys Val Ser Leu Ser Pro Lys Leu Glu
1   5   10   15

Cys Ser Gly Thr Val Met Ala His Cys Ser Leu Asn Leu Leu Gly Ser
            20   25   30

Ser Asn Pro Ser Val Ser Val Pro Gln Val Thr Arg Thr Thr Gly Met
        35   40   45

Cys His His Trp Leu Phe Phe Cys Leu Phe Phe Glu Thr Thr Ser Tyr
    50   55   60

Tyr Val Ala Gln Ala His Leu Lys Leu Leu Gly Ser Ser Asp Pro Pro
65   70   75   80

Ser Ala Ser Ala Ser Gln Asn Ala Cys Asp Tyr Arg Gly Val Ser His
                85   90   95

<210> 39
<211> 76
<212> PRT
<213> Homo sapien

<400> 39

Met Leu Pro Pro Leu Cys Phe Tyr Gln Leu Ser Arg Val Phe Ala Ser
1   5   10   15

Trp Leu Ile Lys Val Leu Val Gly Gly Gly Asn Val Cys Glu Ser Pro
                20   25   30

Gly Asp Asp Asn Pro Thr Trp Phe Asn Ser Pro Thr Gly Gly Ser Pro
            35   40   45

Pro Lys Trp Pro His Arg Gly Asn Pro Gln Ala Leu Leu Ala Leu Tyr
    50   55   60

Cys Cys Val Val Phe Val Val Lys Phe Leu Val Tyr
65   70   75

<210> 40
<211> 146
<212> PRT
<213> Homo sapien

<400> 40

Ala Leu Ile Val Leu Gly Leu Val Leu Leu Ser Val Thr Val Gln Gly
1   5   10   15

Lys Val Phe Glu Arg Cys Glu Leu Ala Arg Thr Leu Lys Arg Leu Gly
                20   25   30

Met Asp Gly Tyr Arg Gly Ile Ser Leu Ala Asn Trp Met Cys Leu Ala
            35   40   45

```
Lys Trp Glu Ser Gly Tyr Asn Thr Arg Ala Thr Asn Tyr Asn Ala Gly
    50              55              60

Asp Arg Ser Thr Asp Tyr Gly Ile Phe Gln Ile Asn Ser Arg Tyr Trp
65              70              75              80

Cys Asn Asp Gly Lys Thr Pro Gly Ala Val Asn Ala Cys His Leu Ser
            85              90              95

Cys Ser Ala Leu Leu Gln Asp Asn Ile Ala Asp Ala Val Ala Cys Ala
            100             105             110

Lys Arg Val Val Arg Asp Pro Gln Gly Ile Arg Ala Trp Val Ala Trp
        115             120             125

Arg Asn Arg Cys Gln Asn Arg Asp Val Arg Gln Tyr Val Gln Gly Cys
    130             135             140

Gly Val
145


<210>  41
<211>  34
<212>  PRT
<213>  Homo sapien

<400>  41

Met Arg Lys Glu Ser Ala Asp Val Gly Tyr Asn Gly Ile Leu Ala Arg
1               5               10              15

Leu Trp Cys Gln Trp Ile Leu His Pro Thr Thr Ser Pro Cys Lys Ala
            20              25              30

Lys Leu


<210>  42
<211>  80
<212>  PRT
<213>  Homo sapien

<400>  42

Met Phe Ala Cys Val Cys Cys Phe Gly Val Trp Cys Val Phe Gly Phe
1               5               10              15
```

31

Gly Val Val Cys Phe Val Phe Thr Leu Trp Phe Val Thr Glu Asn Trp
            20   25   30

Gly Glu Trp Glu Pro Gly Asn Lys Ile Ser Thr Pro Arg Glu Pro Ala
            35   40   45

Phe Gly Pro Gly Tyr Pro Gln Arg Leu Phe Phe Val Phe Cys Cys Val
    50   55   60

Phe Phe Pro Val Asn Thr Lys Glu Gln Ile Phe Ile Glu Leu Val Gln
65   70   75   80

<210> 43
<211> 227
<212> PRT
<213> Homo sapien

<400> 43

Thr Ser Gln Ala Asn Asn Ser Ala Ser Gly His Ser Arg Thr Thr Val
1   5   10   15

Lys Thr Ile Thr Val Ser Ala Asp Val Pro Lys Pro Ser Ile Ser Ser
            20   25   30

Asn Asn Ser Lys Pro Val Glu Asp Lys Asp Ala Val Ala Phe Thr Cys
            35   40   45

Glu Pro Glu Ala Gln Asn Thr Thr Tyr Leu Trp Trp Val Asn Gly Gln
    50   55   60

Ser Leu Pro Val Ser Pro Arg Leu Gln Leu Ser Asn Gly Asn Arg Thr
65   70   75   80

Leu Thr Leu Phe Asn Val Thr Arg Asn Asp Ala Arg Ala Tyr Val Cys
            85   90   95

Gly Ile Gln Asn Ser Val Ser Ala Asn Arg Ser Asp Pro Val Thr Leu
            100   105   110

Asp Val Leu Tyr Gly Pro Asp Thr Pro Ile Ile Ser Pro Pro Asp Ser
    115   120   125

Ser Tyr Leu Ser Gly Ala Asn Leu Asn Leu Ser Cys His Ser Ala Ser
    130   135   140

32

```
Asn Pro Ser Pro Gln Tyr Ser Trp Arg Ile Asn Gly Ile Pro Gln Gln
145                 150             155                 160


His Thr Gln Val Leu Phe Ile Ala Lys Ile Thr Pro Asn Asn Asn Gly
                165             170                 175


Thr Tyr Ala Cys Phe Val Ser Asn Leu Ala Thr Gly Arg Asn Asn Ser
                180             185                 190


Ile Val Lys Ser Ile Thr Val Ser Ala Ser Arg Thr Ser Pro Gly Leu
            195             200             205


Ser Ala Gly Ala Thr Val Gly Ile Met Ile Gly Val Leu Val Gly Val
    210             215             220


Ala Leu Ile
225


<210>   44
<211>   119
<212>   PRT
<213>   Homo sapien

<400>   44

Met Leu Glu Arg Arg Ser Val Met Asp Phe Phe Phe Phe Phe Phe Phe
1               5               10                  15


Phe Phe Phe Phe Phe Phe Phe Phe Phe Phe Leu Asn Pro Phe Phe Ser
            20              25                  30


Pro Pro Gly Gly Gly Val Val Gly Ser Ser Lys His Gln Ala Gln Glu
        35              40              45


Glu Leu Gly Cys Val Pro Phe Leu Ala Ile Val Pro Pro Leu Glu Asn
    50              55              60


Asn Thr Ser Thr Ile Phe His Leu Pro His Lys Ala Gly Gly Cys Thr
65              70              75                  80


Ser Val Ala His Ile Val Val Ile Pro Val Val Cys Lys Ser Gly Leu
            85              90                  95


Leu Arg His Pro Ile Leu Pro Gln Asn Ile Ser Lys Lys Leu His Glu
            100             105                 110
```

His Asn Thr Pro Val Thr Arg
        115

<210>   45
<211>   105
<212>   PRT
<213>   Homo sapien

<400>   45

Met Ser Val Ala Ser Val Pro Leu Gln Cys Asp Asp Val Arg Ser Leu
1   5   10   15

Gln Ala Leu Asn Ala Cys Pro His Met Ser Tyr Leu Cys Cys Gly Thr
            20   25   30

Ser His Arg Gly Gln Ile Val Glu Ile Tyr Arg Val Thr Trp Tyr Leu
        35   40   45

Leu Val Asn Cys Thr Thr Asn Ala Pro Val Tyr Met Gln Cys Ile Gly
    50   55   60

Ile Val Lys Lys Phe Cys Pro Leu Pro Cys Ser His Gly Glu His Asn
65   70   75   80

Arg Gln Phe Ser Ser Pro Val Val His Leu Glu Gln Tyr Thr Ala Leu
                85   90   95

Phe Ala Ile Asn Ile Tyr Arg Asn Ile
            100   105

<210>   46
<211>   79
<212>   PRT
<213>   Homo sapien

<400>   46

Met Gly Pro Arg Leu Ser Gln Arg Pro Gly Ile Pro Pro Ile Leu Ser
1   5   10   15

Asn Asn Val Arg Val Leu Ser Leu Cys Leu Pro Ala Ile Val Ala Thr
            20   25   30

Leu Leu Cys Arg Pro Glu Cys Ala Trp Ser Ser Leu Val Val Ala Leu
        35   40   45

Asn Phe Phe Ser Leu Thr Thr Thr Glu Gly Cys Ala Val Ala Ser Ala

<pre>
          50   55   60

Thr Leu Trp Glu Pro Gln Arg Gly Leu Thr Glu Arg Trp Gly Arg
65   70   75
</pre>

<210> 47
<211> 74
<212> PRT
<213> Homo sapien

<400> 47

<pre>
Met Cys Leu Cys Gly Gly Asp Phe Met Cys Val Gly Arg Gly Ser Asp
1   5   10   15

Thr His Ser Val Cys Arg Thr Pro Pro Gly Gly His Tyr Arg Ser Phe
            20   25   30

Leu Arg Pro Leu Ser Gly Thr Leu Ala Ser Glu Leu Cys Cys Tyr Leu
        35   40   45

Ser Leu Phe Phe Val Cys Phe Leu Tyr Ser Phe Ser Leu Ser Leu Val
    50   55   60

Tyr Gly Gln Asn Ser Ser Arg Leu Ser Met
65   70
</pre>

<210> 48
<211> 59
<212> PRT
<213> Homo sapien

<400> 48

<pre>
Met Phe Cys Gln Cys Cys Ser Cys Val Val Met Val Leu Arg His Leu
1   5   10   15

Thr Ser Ala Phe Phe Ala Val Pro Gly Ala Phe Cys Leu Ala Ser Phe
            20   25   30

Val Ser Thr Cys Cys Leu Ser Val Leu Leu Phe Ser Arg Asp Ser Arg
        35   40   45

Gly Ile Tyr Arg Ile Tyr Arg Leu Phe Asp Val
    50   55
</pre>

<210> 49
<211> 60

<212> PRT
<213> Homo sapien

<400> 49

Met Pro Glu Ser Asn Gly Pro Arg Ser Asp Arg Gln Thr Arg Val Arg
1   5   10   15

Ala Val Ile Arg Ser Ala Val Glu Gly Gly Arg His Val Gln Tyr Asp
            20   25   30

Ala Asp Gln Ile Asp Ala Asn Asn Trp Ser Lys Cys Ser Thr Thr Lys
        35   40   45

Gly Ala Leu Arg Ala Arg Arg His Cys Arg Leu Val
    50   55   60

<210> 50
<211> 1134
<212> PRT
<213> Homo sapien

<400> 50

Arg Leu Ala Leu Ser Pro Glu Asp Lys Pro Ile Arg Leu Ser Pro Ser
1   5   10   15

Lys Ile Thr Glu Pro Leu Arg Glu Gly Pro Glu Glu Glu Pro Leu Ala
            20   25   30

Glu Arg Glu Val Lys Ala Glu Val Glu Asp Met Asp Glu Gly Pro Thr
        35   40   45

Glu Leu Pro Pro Leu Glu Ser Pro Leu Pro Leu Pro Ala Ala Glu Ala
    50   55   60

Met Ala Thr Pro Ser Pro Ala Gly Gly Cys Gly Gly Gly Leu Leu Glu
65   70   75   80

Ala Gln Ala Leu Ser Ala Thr Gly Gln Ser Cys Ala Glu Pro Ser Glu
                85   90   95

Cys Pro Asp Phe Val Glu Gly Pro Glu Pro Arg Val Asp Ser Pro Gly
            100   105   110

Arg Thr Glu Pro Cys Thr Ala Ala Leu Asp Leu Gly Val Gln Leu Thr
        115   120   125

36

```
Pro Glu Thr Leu Val Glu Ala Lys Glu Glu Pro Val Glu Val Pro Val
    130                 135             140

Gly Val Pro Val Val Glu Ala Val Pro Glu Glu Gly Leu Ala Gln Val
145                 150             155                 160

Ala Pro Ser Glu Ser Gln Pro Thr Leu Glu Met Ser Asp Cys Asp Val
            165             170             175

Pro Ala Gly Glu Gly Gln Cys Pro Ser Leu Glu Pro Gln Glu Ala Val
            180             185             190

Pro Val Leu Gly Ser Thr Cys Phe Leu Glu Glu Ala Ser Ser Asp Gln
        195             200             205

Phe Leu Pro Ser Leu Glu Asp Pro Leu Ala Gly Met Asn Ala Leu Ala
    210             215             220

Ala Ala Ala Glu Leu Pro Gln Ala Arg Pro Leu Pro Ser Pro Gly Ala
225             230             235             240

Ala Gly Ala Gln Ala Leu Glu Lys Leu Glu Ala Ala Glu Ser Leu Val
            245             250             255

Leu Glu Gln Ser Phe Leu His Gly Ile Thr Leu Leu Ser Glu Ile Ala
            260             265             270

Glu Leu Glu Leu Glu Arg Arg Ser Gln Glu Met Gly Gly Ala Glu Arg
        275             280             285

Ala Leu Val Ala Arg Pro Ser Leu Glu Ser Leu Leu Ala Ala Gly Ser
    290             295              300

His Met Leu Arg Glu Val Leu Asp Gly Pro Val Val Asp Pro Leu Lys
305             310             315             320

Asn Leu Arg Leu Pro Arg Glu Leu Lys Pro Asn Lys Lys Tyr Ser Trp
            325             330             335

Met Arg Lys Lys Glu Glu Arg Met Tyr Ala Met Lys Ser Ser Leu Glu
        340             345             350

Asp Met Asp Ala Leu Glu Leu Asp Phe Arg Met Arg Leu Ala Glu Val
    355             360             365
```

37

```
Gln Arg Gln Tyr Lys Glu Lys Gln Arg Glu Leu Val Lys Leu Gln Arg
    370             375             380

Arg Arg Asp Ser Glu Asp Arg Arg Glu Glu Pro His Arg Ser Leu Ala
385             390             395             400

Arg Arg Gly Pro Gly Arg Pro Arg Lys Arg Thr His Ala Pro Ser Ala
            405             410             415

Leu Ser Pro Pro Arg Lys Arg Gly Lys Ser Gly His Ser Ser Gly Lys
            420             425             430

Leu Ser Ser Lys Ser Leu Leu Thr Ser Asp Asp Tyr Glu Leu Gly Ala
    435             440             445

Gly Ile Arg Lys Arg His Lys Gly Ser Glu Glu Glu His Asp Ala Leu
    450             455             460

Ile Gly Met Gly Lys Ala Arg Gly Arg Asn Gln Thr Trp Asp Glu His
465             470             475             480

Glu Ala Ser Ser Asp Phe Ile Ser Gln Leu Lys Ile Lys Lys Lys Lys
            485             490             495

Met Ala Ser Asp Gln Glu Gln Leu Ala Ser Lys Leu Asp Lys Ala Leu
            500             505             510

Ser Leu Thr Lys Gln Asp Lys Leu Lys Ser Pro Phe Lys Phe Ser Asp
    515             520             525

Ser Ala Gly Gly Lys Ser Lys Thr Ser Gly Gly Cys Gly Arg Tyr Leu
    530             535             540

Thr Pro Tyr Asp Ser Leu Leu Gly Lys Asn Arg Lys Ala Leu Ala Lys
545             550             555             560

Gly Leu Gly Leu Ser Leu Lys Ser Ser Arg Glu Gly Lys His Lys Arg
            565             570             575

Ala Ala Lys Thr Arg Lys Met Glu Val Gly Phe Lys Ala Arg Gly Gln
            580             585             590

Pro Lys Ser Ala His Ser Pro Phe Ala Ser Glu Val Ser Ser Tyr Ser
```

```
                595                     600                     605


Tyr Asn Thr Asp Ser Glu Glu Asp Glu Glu Phe Leu Lys Asp Glu Trp
    610                 615                 620


Pro Ala Gln Gly Pro Ser Ser Ser Lys Leu Thr Pro Ser Leu Leu Cys
625                 630                 635                 640


Ser Met Val Ala Lys Asn Ser Lys Ala Ala Gly Gly Pro Lys Leu Thr
                645                 650                 655


Lys Arg Gly Leu Ala Ala Pro Arg Thr Leu Lys Pro Lys Pro Ala Thr
            660                 665                 670


Ser Arg Lys Gln Pro Phe Cys Leu Leu Leu Arg Glu Ala Glu Ala Arg
        675                 680                 685


Ser Ser Phe Ser Asp Ser Ser Glu Glu Ser Phe Asp Gln Asp Glu Ser
    690                 695                 700


Ser Glu Glu Glu Asp Glu Glu Glu Leu Glu Glu Glu Asp Glu Ala
705                 710                 715                 720


Ser Gly Gly Gly Tyr Arg Leu Gly Ala Arg Glu Arg Ala Leu Ser Pro
                725                 730                 735


Gly Leu Glu Glu Ser Gly Leu Gly Leu Leu Ala Arg Phe Ala Ala Ser
            740                 745                 750


Ala Leu Pro Ser Pro Thr Val Gly Pro Ser Leu Ser Val Val Gln Leu
        755                 760                 765


Glu Ala Lys Gln Lys Ala Arg Lys Lys Glu Glu Arg Gln Ser Leu Leu
    770                 775                 780


Gly Thr Glu Phe Glu Tyr Thr Asp Ser Glu Ser Glu Val Lys Val Arg
785                 790                 795                 800


Lys Arg Ser Pro Ala Gly Leu Leu Arg Pro Lys Lys Gly Leu Gly Glu
                805                 810                 815


Pro Gly Pro Ser Leu Ala Ala Pro Thr Pro Gly Ala Arg Gly Pro Asp
                820                 825                 830
```

39

```
Pro Ser Ser Pro Asp Lys Ala Lys Leu Ala Val Glu Lys Gly Arg Lys
        835             840             845


Ala Arg Lys Leu Arg Gly Pro Lys Glu Pro Gly Phe Glu Ala Gly Pro
    850             855             860


Glu Ala Ser Asp Asp Asp Leu Trp Thr Arg Arg Arg Ser Glu Arg Ile
865             870             875             880


Phe Leu His Asp Ala Ser Ala Ala Ala Pro Ala Pro Val Ser Thr Ala
            885             890             895


Pro Ala Thr Lys Thr Ser Arg Cys Ala Lys Gly Gly Pro Leu Ser Pro
            900             905             910


Arg Lys Asp Ala Gly Arg Ala Lys Asp Arg Lys Asp Pro Arg Lys Lys
        915             920             925


Lys Lys Gly Lys Glu Ala Gly Pro Gly Ala Gly Leu Pro Pro Pro Arg
    930             935             940


Ala Pro Ala Leu Pro Ser Glu Ala Arg Ala Pro Pro Pro Pro Pro
945             950             955             960


Pro Pro Pro His Pro Pro Leu Pro Pro Pro Leu Pro Pro Pro Pro
            965             970             975


Leu Pro Leu Arg Leu Pro Pro Leu Pro Pro Pro Leu Pro Arg Pro
        980             985             990


His Pro Pro Pro Pro Pro Pro Leu Pro Pro Leu Leu Pro Pro Pro Gln
        995             1000            1005


Thr Arg  Thr Leu Pro Ala Ala  Arg Thr Met Arg Gln  Pro Pro Pro
    1010            1015            1020


Pro Arg  Leu Ala Leu Pro Arg  Arg Arg Arg Ser Pro  Pro Arg Pro
    1025            1030            1035


Pro Ser  Arg Pro Ala Arg Arg  Gly Pro Arg Pro Thr  Pro Gln Ala
    1040            1045            1050


Arg Arg  Arg Pro Arg Pro Ser  Pro Arg Arg Leu Leu  Arg Ser Pro
    1055            1060            1065
```

```
His Ser  Leu Cys Ser Pro Arg  Leu Arg Pro Gly Pro  Arg Ala Asp
    1070            1075            1080


Pro Arg  Arg Glu Arg Ala Ser  Thr Ser Pro Pro Pro  Arg Ser Trp
    1085            1090            1095


Pro Ser  Gly Ser Ala Cys Arg  Pro Trp Arg Thr Gly  Pro Arg Ser
    1100            1105            1110


Pro Pro  Ser Cys Gln Pro Gly  Ser Ser Gly Ser Gly  Ser Ala Ser
    1115            1120            1125


Pro Pro  Ser Gly Val Ala
    1130
```

```
<210>   51
<211>   29
<212>   PRT
<213>   Homo sapien


<400>   51


Met Gly Arg Cys Val Ser Leu Thr Ser Val Ile Ile Phe Asp Ile Leu
1               5               10              15


Ser Val Tyr Tyr Glu Thr Leu Ala Ser Leu Gln Ile Phe
            20              25
```

```
<210>   52
<211>   161
<212>   PRT
<213>   Homo sapien


<400>   52


Val Ala Ile Pro Pro Leu Thr His Asn Leu Ser Ala Val Ala Pro Ser
1               5               10              15


Ile Asn Ser Gly Met Gly Thr Glu Thr Ile Pro Ile Gln Gly Tyr Arg
            20              25              30


Val Asp Glu Lys Thr Lys Lys Cys Ser Ile Pro Phe Val Lys Pro Asn
        35              40              45


Arg His Ser Pro Ser Gly Ile Tyr Asn Ile Asn Val Thr Thr Leu Val
    50              55              60
```

```
Ser Ser Glu Lys Asn Leu Leu Trp Ala Ser Lys Lys Arg Arg Glu Tyr
65              70              75                  80


Ser Arg Thr Asp Val Arg Leu Pro Glu Leu Asn Tyr Asn His Leu Pro
            85              90                  95


Glu Leu Arg Ala Leu Gly Gly Ile Ala Arg Asn Ser Arg Leu Thr Lys
            100             105             110


Lys Glu Ser Lys Ile Leu Ser Glu Ser Arg Ile Pro Ser Leu Ala Ala
        115             120             125


Ile Asp Leu His Thr Pro Ser Ile Thr Leu His Gln Val Ser Gly Pro
    130             135             140


Pro Leu Ser Asp Asp Ser Gly Ala Asp Leu Pro Gln Met Glu His Gln
145             150             155             160


His
```

```
<210>  53
<211>  33
<212>  PRT
<213>  Homo sapien

<400>  53

Met Asn Tyr Cys Leu Lys Thr Ser Ser Thr Ser Gln Ser Thr Thr Ala
1               5               10              15


Thr Ser Ile Cys Lys Asn His Tyr Leu Leu Tyr Val Leu Trp Tyr Leu
            20              25              30


Gly
```

```
<210>  54
<211>  89
<212>  PRT
<213>  Homo sapien

<400>  54

Met Val Ser Ile Lys Ser Leu Leu Phe Glu Ser Tyr Val His Gly Pro
1               5               10              15


Ala Val Val Arg Phe Ser Ala Leu Gln Leu Pro Asp Thr Phe Gly Arg
```

```
                    20                        25                        30


        Pro Met Ala Glu Arg Thr Arg Leu Ser Pro Gly Val Arg Ala Pro Ala
                35                  40                  45


        Trp Ala Thr Tyr Val Gly Thr Pro Ser Arg Gly Phe Leu Leu Leu Tyr
                50                  55                  60


        Glu Lys Lys Gln Ile Ser Val Ala Lys Thr Leu Leu Gln Thr Thr Arg
        65                  70                  75                  80


        Glu Ala His Arg Asn Thr Val Ser Tyr
                        85
```

<210> 55
<211> 110
<212> PRT
<213> Homo sapien

<400> 55

```
        Met Val Gln His Arg Cys Met Leu Glu Arg Arg Val Val Met Asp Ala
        1                   5                  10                  15


        Trp Ser Arg Pro Arg Tyr Ser Thr Ser Asn Phe Pro Arg Asn Gln Lys
                        20                  25                  30


        Asn Gly Glu Gln Val Leu Val Ser Gln Tyr Ser Ala Ser Val Tyr Thr
                        35                  40                  45


        Leu Gly Gln Gly Gln Ile Phe Pro Gly Glu Gly Phe Tyr His Cys His
                        50                  55                  60


        His Leu Glu Ile Leu His Arg Leu Glu His Arg Ala Ile Asp Phe His
        65                  70                  75                  80


        Phe Cys Thr Gln Leu Cys Ser Glu Thr Gly Ala Ile Gly Val Leu Gly
                        85                  90                  95


        Glu Thr Gly Gln Met Glu Glu Val Glu Gly Ile Cys Thr Leu
                        100                 105                 110
```